

[illegible]

### Figure 1B

[illegible]

**Figure 1C**

[illegible]

[illegible]

[illegible]

Figure 1f

<sup>26</sup>  
 A V T M I O R P K G L A F T O V O V O S I K I A M E S P O G O V S R Y R V T T S  
 T C A G T A A C C A C A T T G A T C C C C T A A G G A C T T C A T T C A T T G C A T T C A A A T T C C T T C C A A G C C A C A C C C C A G T T T C C A G G T A C A G G T A C T A C T C  
 4810 4820 4830 4840 4850 4860 4870 4880 4890 4900 4910 4920  
  
 S P E O G I M E L F P A P O G E E O T A E L O G L R P G S E Y T V S Y V A L M D  
 G A T C C T G A G G A T E R A A T C C A T T A C T T A C C T G A T G T G A G A G A C A C T C A G A G C T C A A G C C T C A G A C C C G G T C T C A G T A C A C A G T C A G T G C T T C C C T T C C A C C A  
 4930 4940 4950 4960 4970 4980 4990 5000 5010 5020 5030 5040  
  
<sup>27</sup>  
 O M E S Q P L I G T O S T A I P A P T O L K F T O V T P T S L S A Q M T P P M V  
 T G A T A G G A G A C C C C C T G A T T G A C C C A G T T C C A C A C T A T T C C T C C A C A C T A C C T C A G G T C A G G T C A G A C C C A C A G C C T G A C C C C C A G T C C A C A C C C C A G T  
 5050 5060 5070 5080 5090 5100 5110 5120 5130 5140 5150 5160  
  
 O L T G Y R V R V T P K E K T G P M K E I M L A P O S S S V V S G L M V A T K  
 T C A C T C A C T G A T C G A G T C C C C G T G A C C C A G A G A C C C A C C A T T A C A G A A T C A G C T T C T C A G A C T C A T C G T T G T A T C A G A C T T A T G G T C C C A C C A A  
 5170 5180 5190 5200 5210 5220 5230 5240 5250 5260 5270 5280  
  
<sup>28</sup>  
 Y E V S V Y A L K O T L T S R P A O G V V T T L E M V S P P R M A R V T O A T E  
 A T A T G A G T C A G T G T A T G C T G T A A G C A C A C T T T G A C A G C A G A C C A C T C A C C G T T G T G T C A C A C T C A T C A G A A I G T C A G C C C A C C A G A G A G C C T G T G T C A C A G A T G C T A C A  
 5290 5300 5310 5320 5330 5340 5350 5360 5370 5380 5390 5400  
  
 T T I T I S M R T K T E T I T G F O V O A V P A M G O T P I Q R T I K P O V R S  
 G A C C A C A T C A C C A T T A G C T G A G A C A C A C T G A G A G A T C A C T G C T T C C A G T T G A I G C C G T T C A G C C A A T T C C C A C A C T C C A A T C C A G A G A C C A T C A G C C A G A T G C A G A G  
 5410 5420 5430 5440 5450 5460 5470 5480 5490 5500 5510 5520  
  
<sup>29</sup>  
 Y T I T G L O P G T O Y K I Y L Y T L M O N A R S S P V V I D A S T A I O A P S  
 C T A C A C A T C A C A G G T T T A C A A C C A G C A C T G A C T A C A G A T C T A C T G T A C A C A T T C A T T G A C A C A T T C C C G C T C C C G C T C C C G C T C C C G C T C C C A C C A C C A C  
 5530 5540 5550 5560 5570 5580 5590 5600 5610 5620 5630 5640  
  
 M L R F L A T T P M S L L V S M O P P R A R I T G T I K Y E K P G S P R E V  
 C A C C T C C C T T T C C T G C C A C C A C A C C A C A C T T T C C T T T T T C C T A T T C A T T G C A G C C C A C C A G T A A C C C C T A C A T C A G A T A C A G A C C T C C G G T C T C T C C A G A A A C T  
 5650 5660 5670 5680 5690 5700 5710 5720 5730 5740 5750 5760

[illegible]

## Figure 1H

36  
G K T Y N V G E Q W Q R E Y L G A I C S C T C F G G Q R G V R C D M C R P C G  
TGBAAGACATACCACTAGBAGAACAGTBBACAGAGBAAATATC TGBBTRCCATTGCTTCTTBCACATGCTTTTGGAGCCACCGGCGC TGBAACTTGGCAGACCTTGGG  
6730 6740 6750 6760 6770 6780 6790 6800 6810 6820 6830 6840  
E P S P E G T F G Q S Y N Q Y S Q R Y N Q R Y N F N V M C P I E C F M P L D V Q  
TGAOCCAGTODGAAOZCAGTACTGGCCAGTCC TACAACCAGTAATCTCABAGATACCATCAGAGAAACACATAATGTTAAI TDDCAATTEAGTGTCTCATDCTTTAGATGTCAC  
6850 6860 6870 6880 6890 6900 6910 6920 6930 6940 6950 6960  
A D R E O S R E  
GGCTCAGACAGAGAGATTODGAGAGTAAATCATGTTTDCATTCGAGGAGCAAGCATGTCGTC TDCCAAGATCCATC TAACTGCAGTGAATGT TACGACGCCAGCTTAGAGTCTCT  
6970 6980 6990 7000 7010 7020 7030 7040 7050 7060 7070 7080  
TTTCTTTCTTAAGDCTTTGCTCTGAGAGAGTTCCTGAGCTTCAGCTCAACTCAGCTTCTGCAAGCATTCAGCTGGAGGTTTCTGAGGAGTTTCTCA TAAATGAGGGCTGCACATT  
7090 7100 7110 7120 7130 7140 7150 7160 7170 7180 7190 7200  
GDCIGTTTCCTTGGAGTAFTCAATADGZCTGAGTAATTTAAATGAGTGAATCTAGAGATTGGTTTGGGATCAATAGCAAGCATATCCAGCAAGCAAGATGCAATGTTTTCATAAT  
7210 7220 7230 7240 7250 7260 7270 7280 7290 7300 7310 7320  
GATATGACCAAAATTTTAACTAGGAAAGTCAOCCAAACACTTC TCTTTTCACTTAAGTGTCTGGGCGGCAATAGCTGAGCAAGCAAGCAATGATCTTGT TACTGTGTAATTT TAAATATDCA  
7330 7340 7350 7360 7370 7380 7390 7400 7410 7420 7430 7440  
CAGTACTCACTTTTCCCAATGATCTAGTAATGGCTAGAAATATCTTCTTCTTACCTGTATTTATCAATTTTTCACGATTTT TTA TACGCAAAAGATGTAAT TCAAAACACTTAGT  
7450 7460 7470 7480 7490 7500 7510 7520 7530 7540 7550 7560  
ATGCGATTGATAGAGCAATTTGGTATATATATGTTGGCTGATTAATTTT TATAC TGTATGTCGCAAGGCTT TACTGCTGCAAGCAAC TGTTT TAA TAAAGATT TACAT TCCACA  
7570 7580 7590 7600 7610 7620 7630 7640 765 7660 7670 7680  
AAAAAAAAAAAAAAAAAAAA  
1690 1700 1710 1720 173 174 175 176 177 178 179 180  
0949297A - 0127001



Figure 2A

Pair 1  
 0 1 5'- AATTCATATGCAGGCACAGCAAAATGGTTACGCCCCAGTCCCGGTGGCTGTCAGTCAAGCAAGCCCGTT - 3'  
 0 2 3'- GTATACGTCGCGTGCGTTTACCAGTCCGGGTACAGGGGCCACCGACAGTCAGTTTCGTTCCGGGCCAACACAATA - 5'

Pair 2  
 0 3 5'- GTTATGACAAATGGAAACACTATCAGATAAATCAACAGTGGGAGCGGACCCTACCTAGGTAATGTGTG - 3'  
 0 4 3'- CTGTTACCTTTTGTGATAGTCTATTTAGTTGTACCCCTCGGCTGGATGGATCCATT - 5'

Pair 3  
 0 5 5'- GTTTGTACTTGTATGGAGGAGCCGAGGTTTAACTGCGAAGTAAACCTGAAGCT - 3'  
 0 6 ACACAACCAACATGACAAATACCTCCTTCGGTCCAAATTGACGCTTTCATTGGACITCGACTTCT - 5'

Pair 4  
 0 7 5'- GAAGAGACTTGCTTTGACAAAGTACACTGGGAACACTTACCGAGTGGGTGACACTTATGAGCGTCTCTAAA - 3'  
 0 8 3'- GAACGAACCTGTTCAATGTGACCTTGTGATGGCTACCCCACTGTGATACTCCGAG - 5'

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Figure 2B

Pair 5

09 5'- GACTCCATGATCTGGGACTGTACCTGCATCGGGGCTGGGCGAGGGAGATAGCTGTACC - 3'  
010 GATTCTGAGGTACTAGACCCCTGACATGGACGTAGCCCCGACCCGCTCCCTCTTATTC - 5'

Pair 6

011 5'- ATGCCCAACGCTGCCATGANGGGGTGAGTCTCCTACCAGATTGGTGACACCTGGAGGAGACCACATGAGACT - 3'  
012 GACATGGTAGCGTTTGGGACGGTACTTCCCCCAGTCAGGATGGTCTAACCCACCTGTGGACCTCCTCTGGTGATCTCTGALCACCACAA - 5'

Pair 7

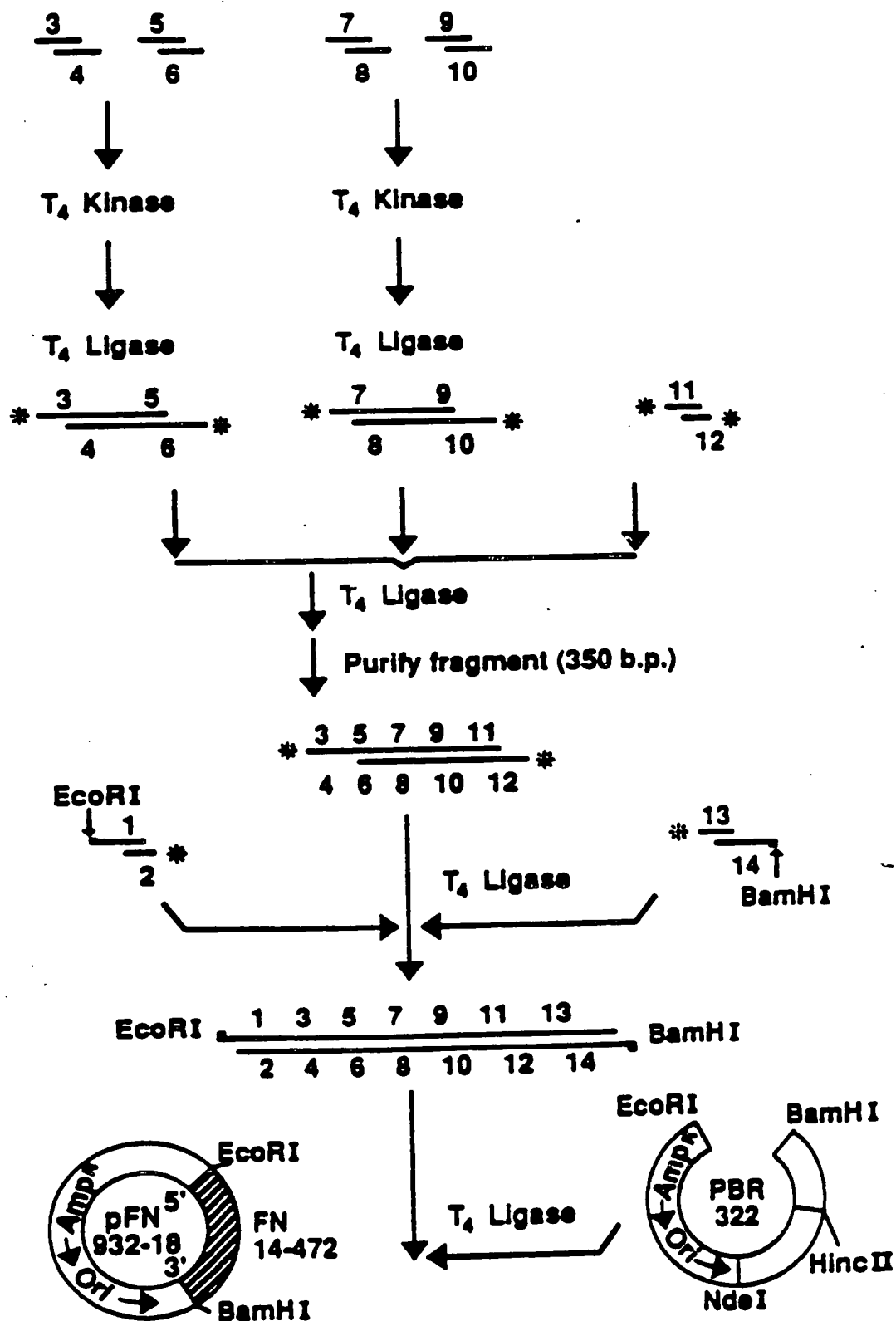
013 5'- GGTGGTTACATGTTAGAGTGTGTGTCTTGGTATGGAAAGGAGATGGACCTGCAGCCCATAGCTGAG - 3'  
014 3'- TGTACAATCTCACACACACAGAACCATTACCTTTTCCCTTACCTGGACGTTTCGGGTATCGGACTCCTAG - 5'

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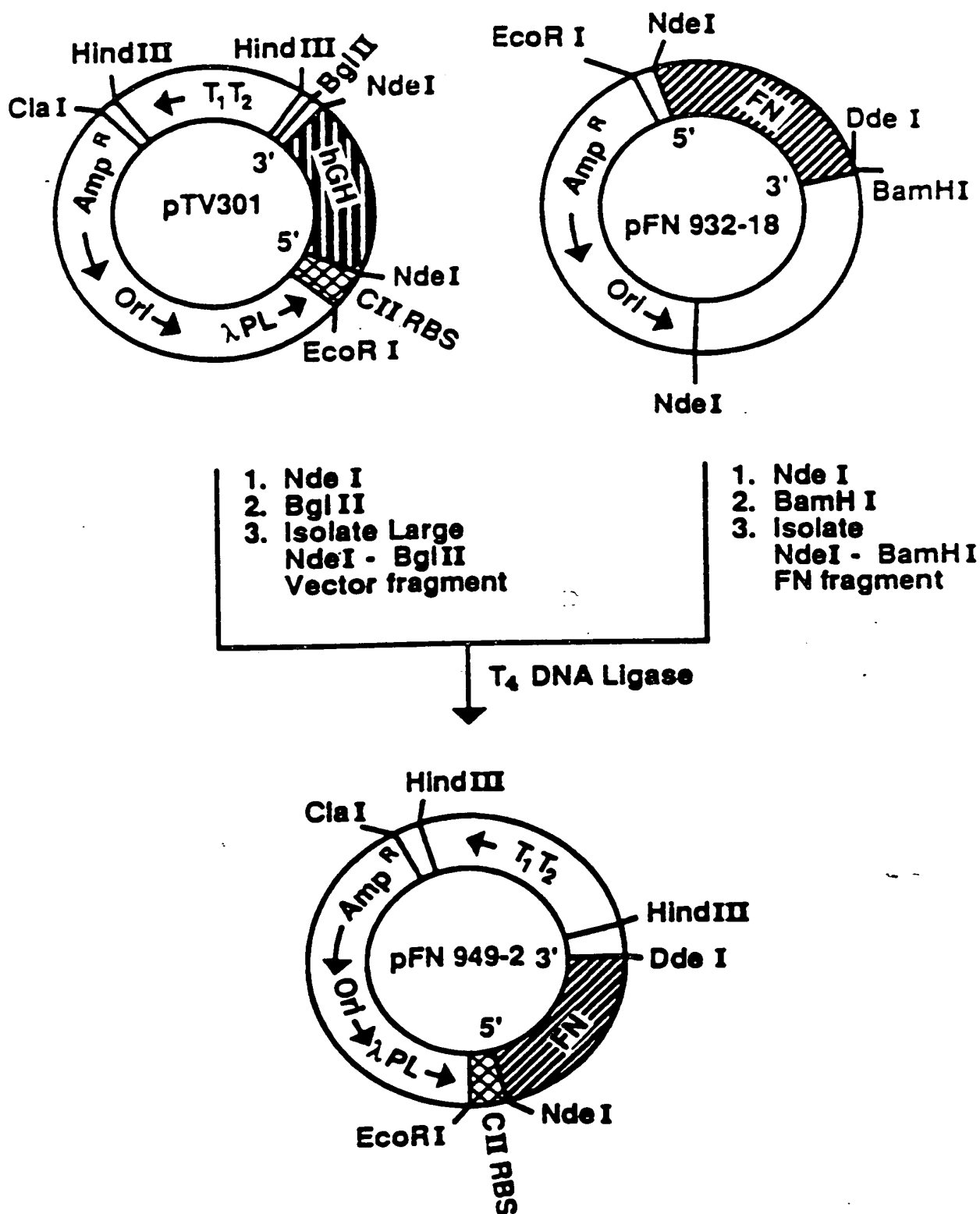
Figure 3

Synthesis of F.N. Gene (14 - 472 b.p.)



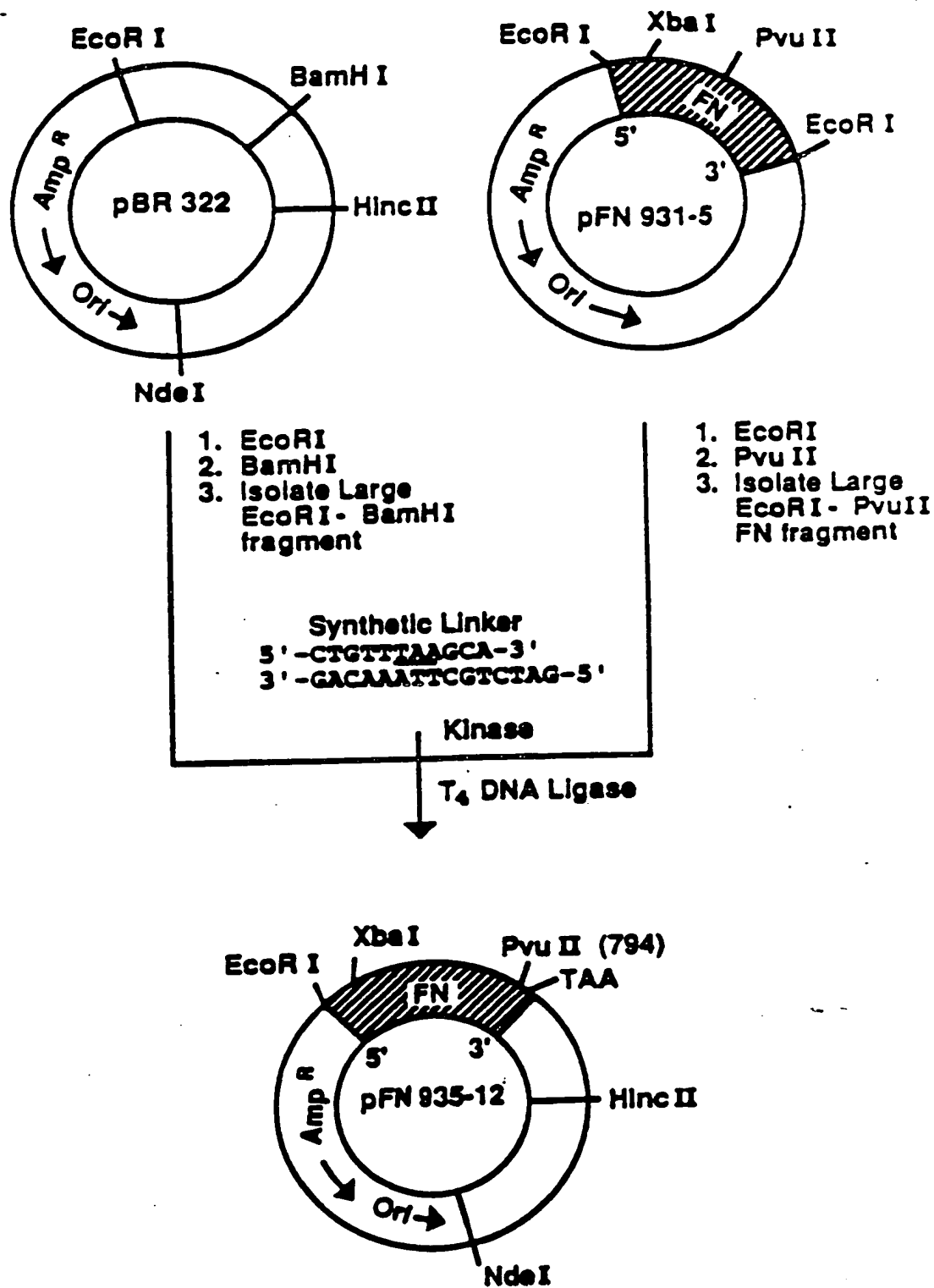
002270-12525460

Figure 4



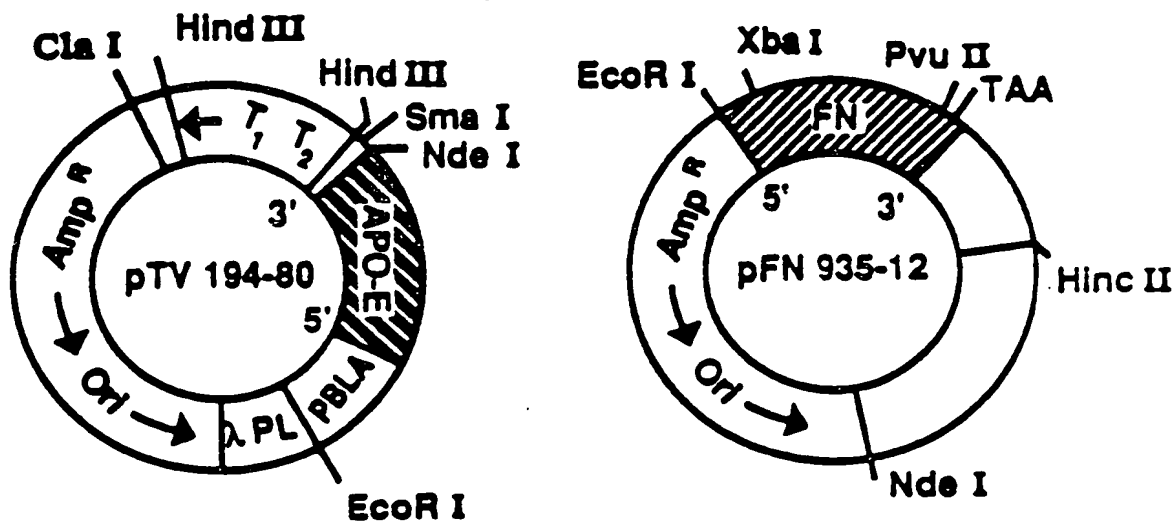
002240-1-012700

Figure 5



00492971.012700

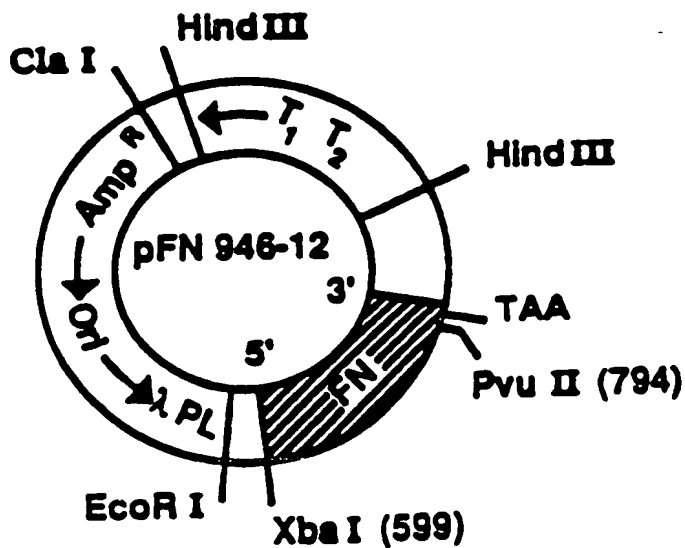
Figure 6



1. EcoR I
2. Sma I
3. Isolate large  
EcoR I - Sma I fragment

1. EcoR I
2. Hinc II
3. Isolate  
EcoR I - Hinc II  
FN fragment

T<sub>4</sub> DNA Ligase



002270-1.012700

Figure 7

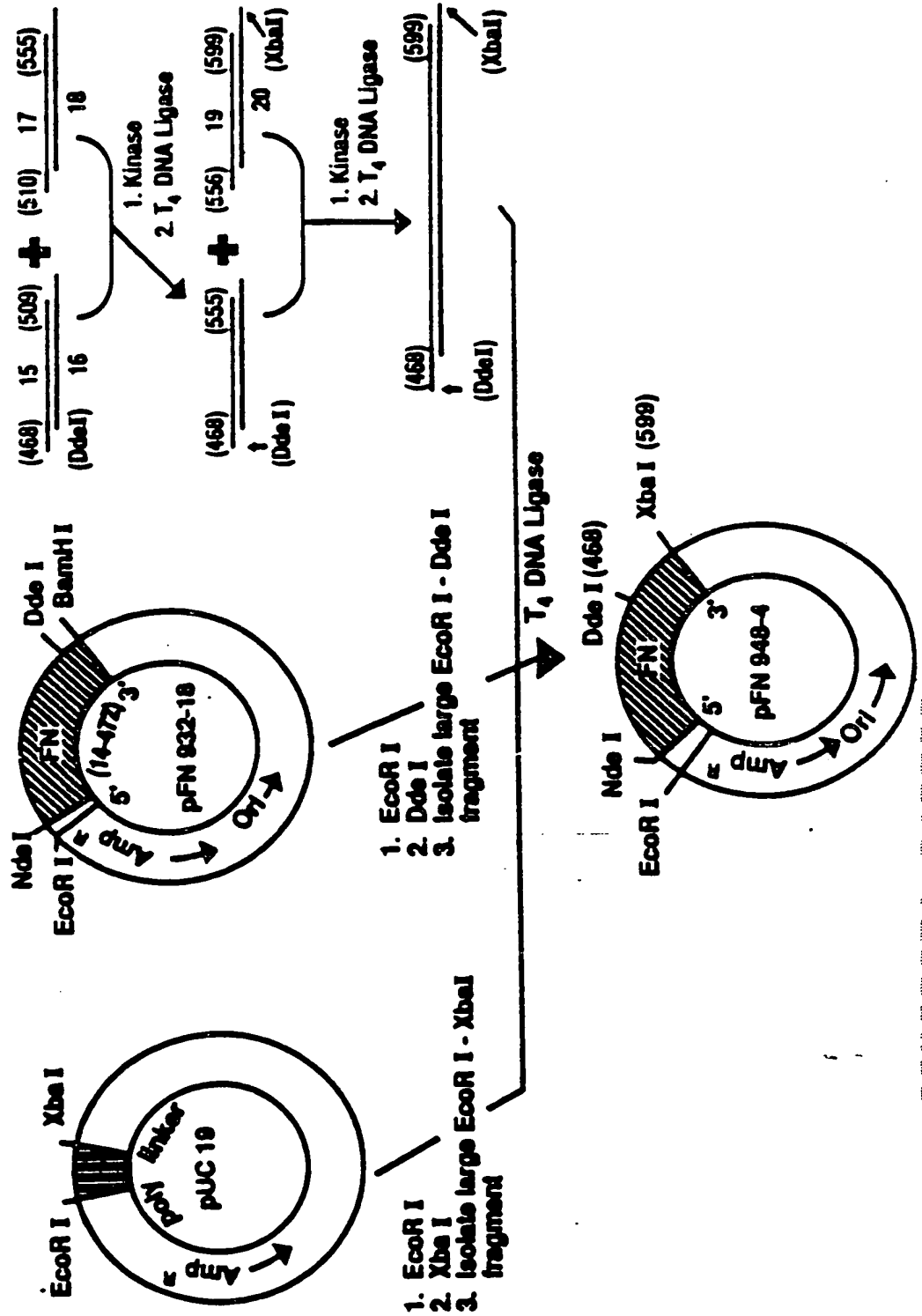
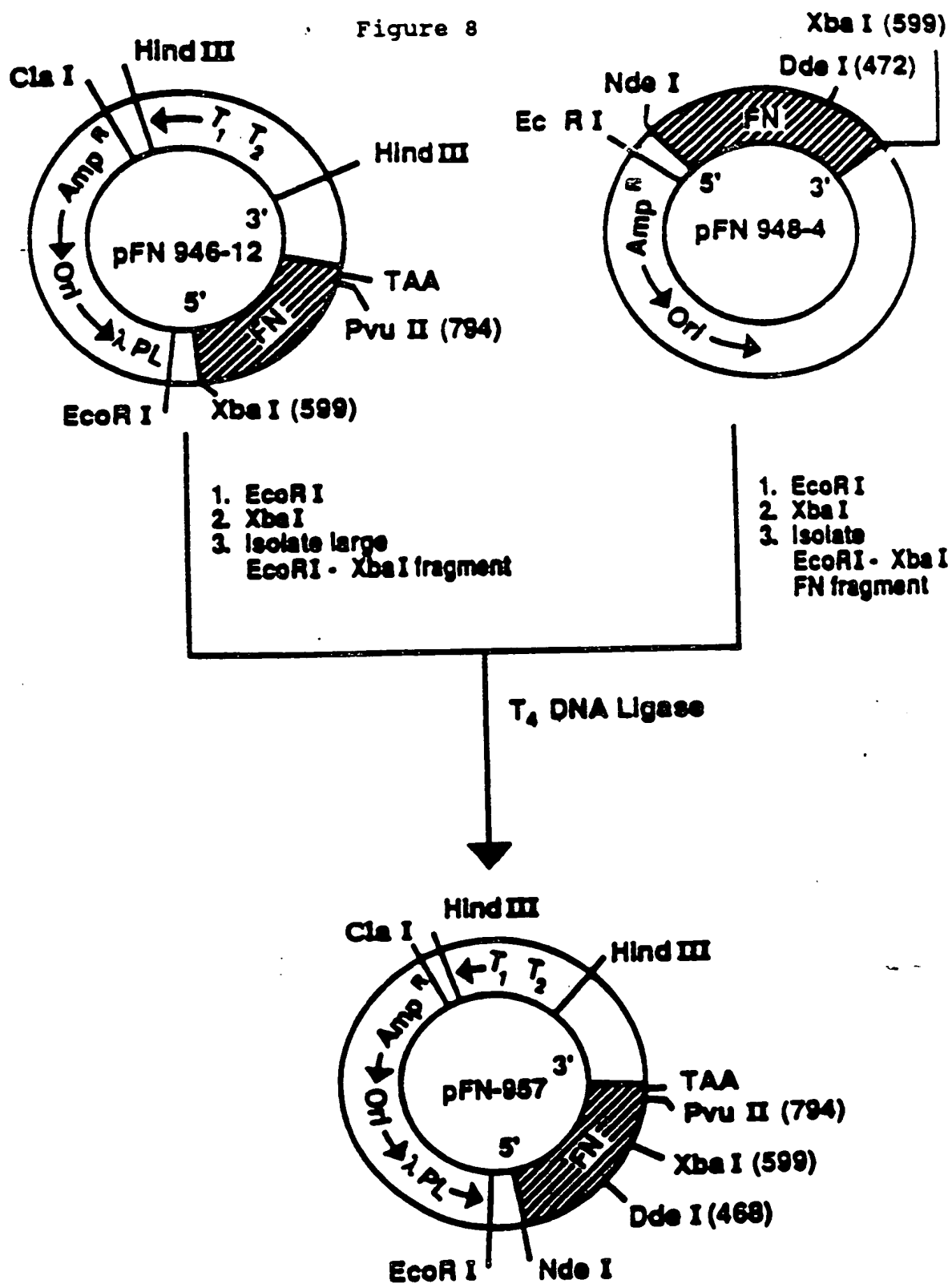


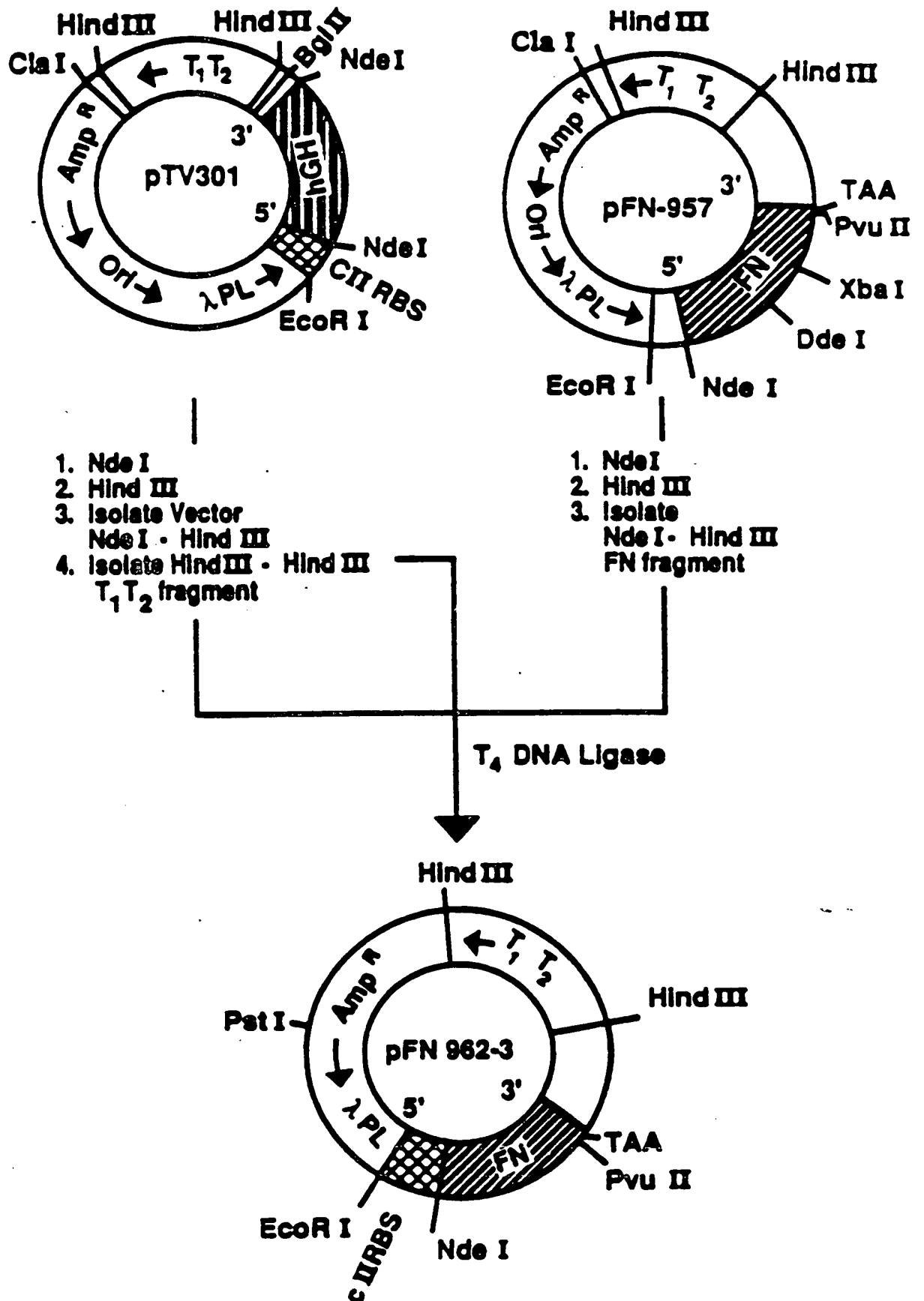
Figure 8



004991.012700

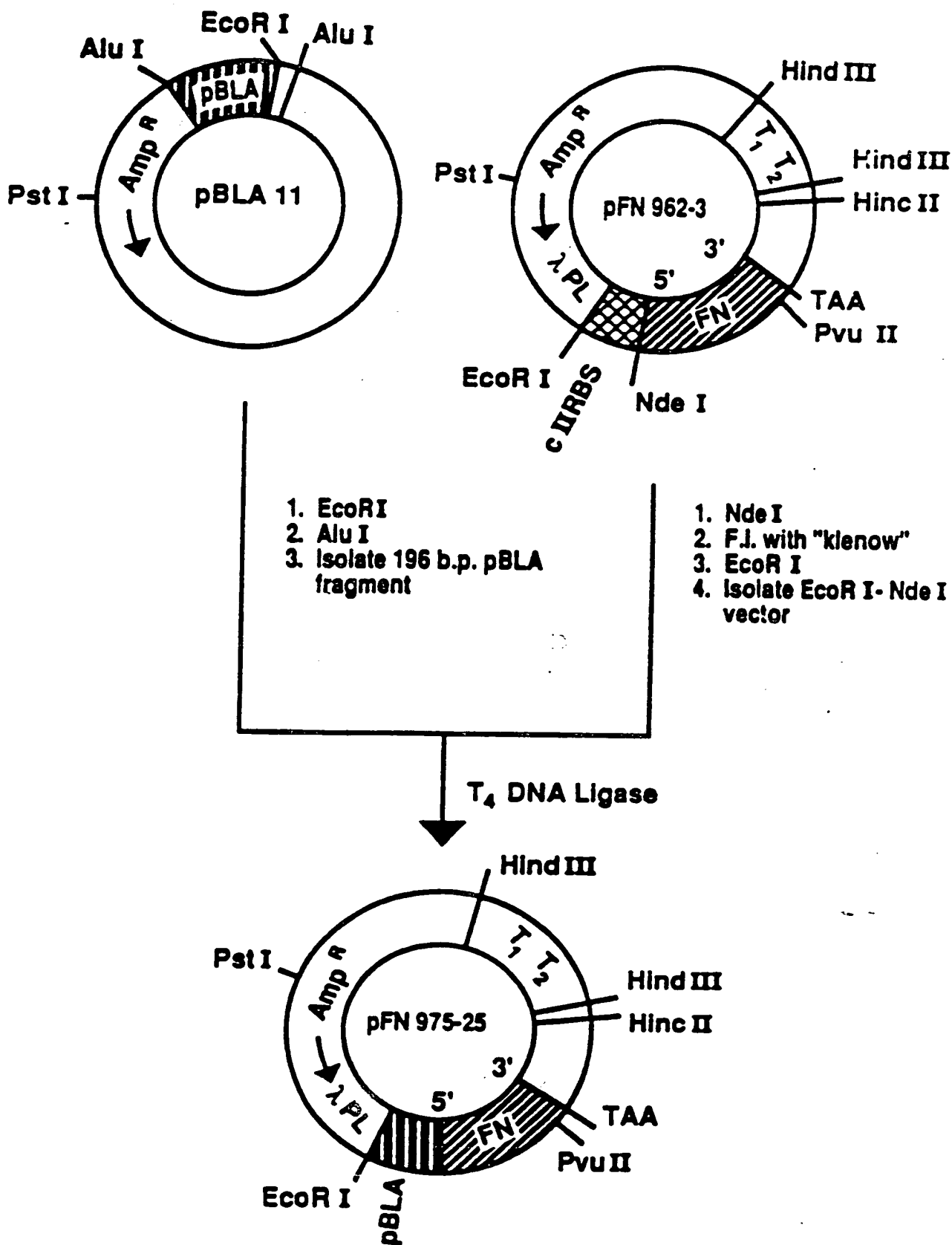


Figur 9



002210" T/626460

Figure 10



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Figure 11

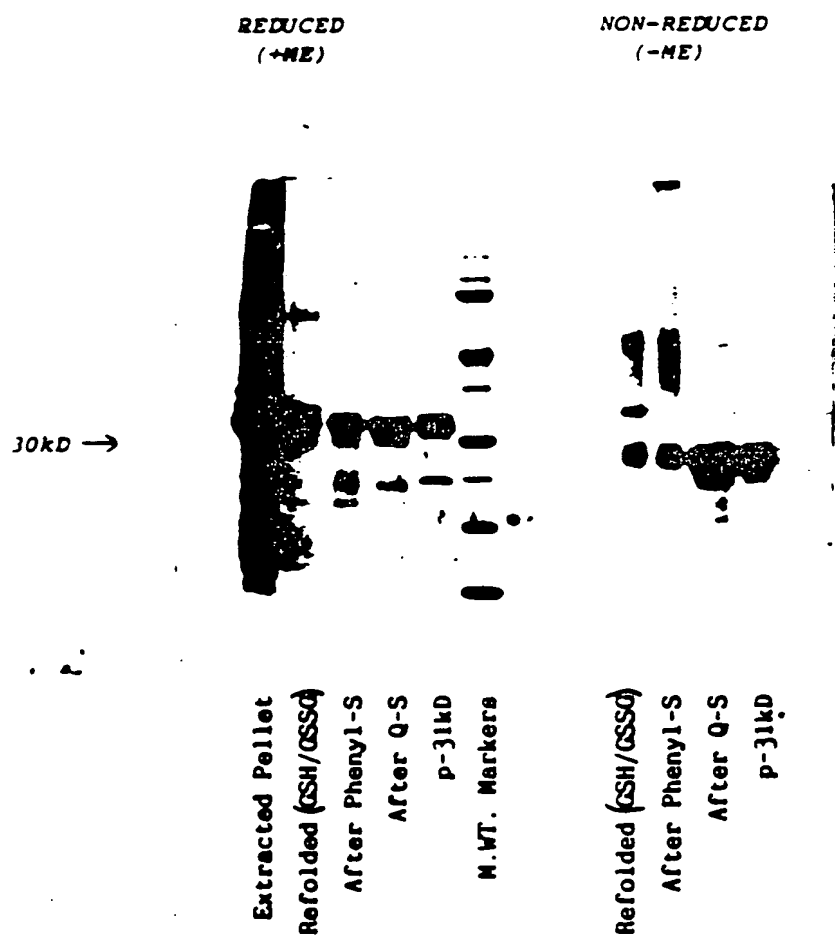


Figure 12

# 31kD / Phenyl-Sepharose

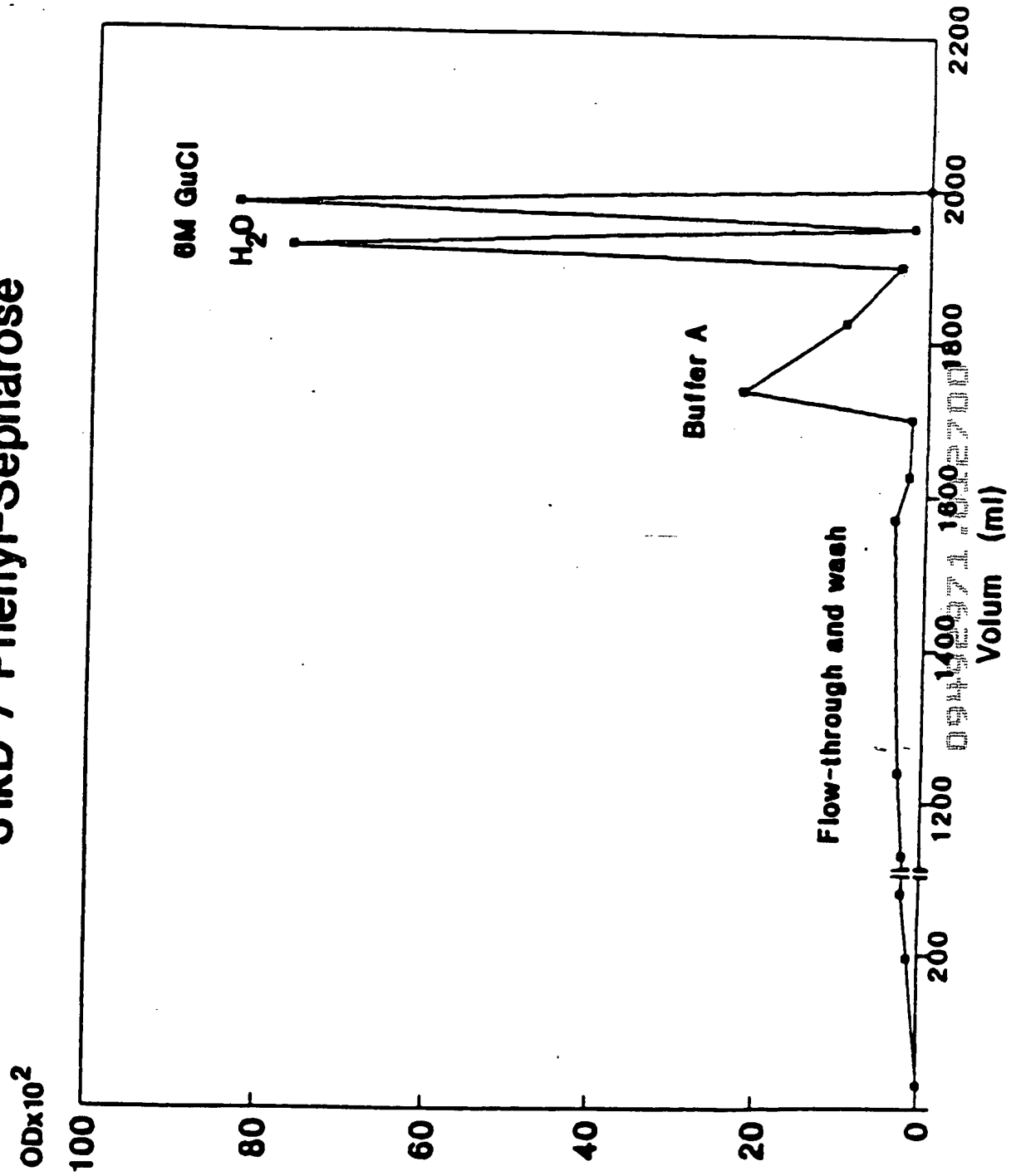


Figure 13  
31kD/Heparin-Sepharose

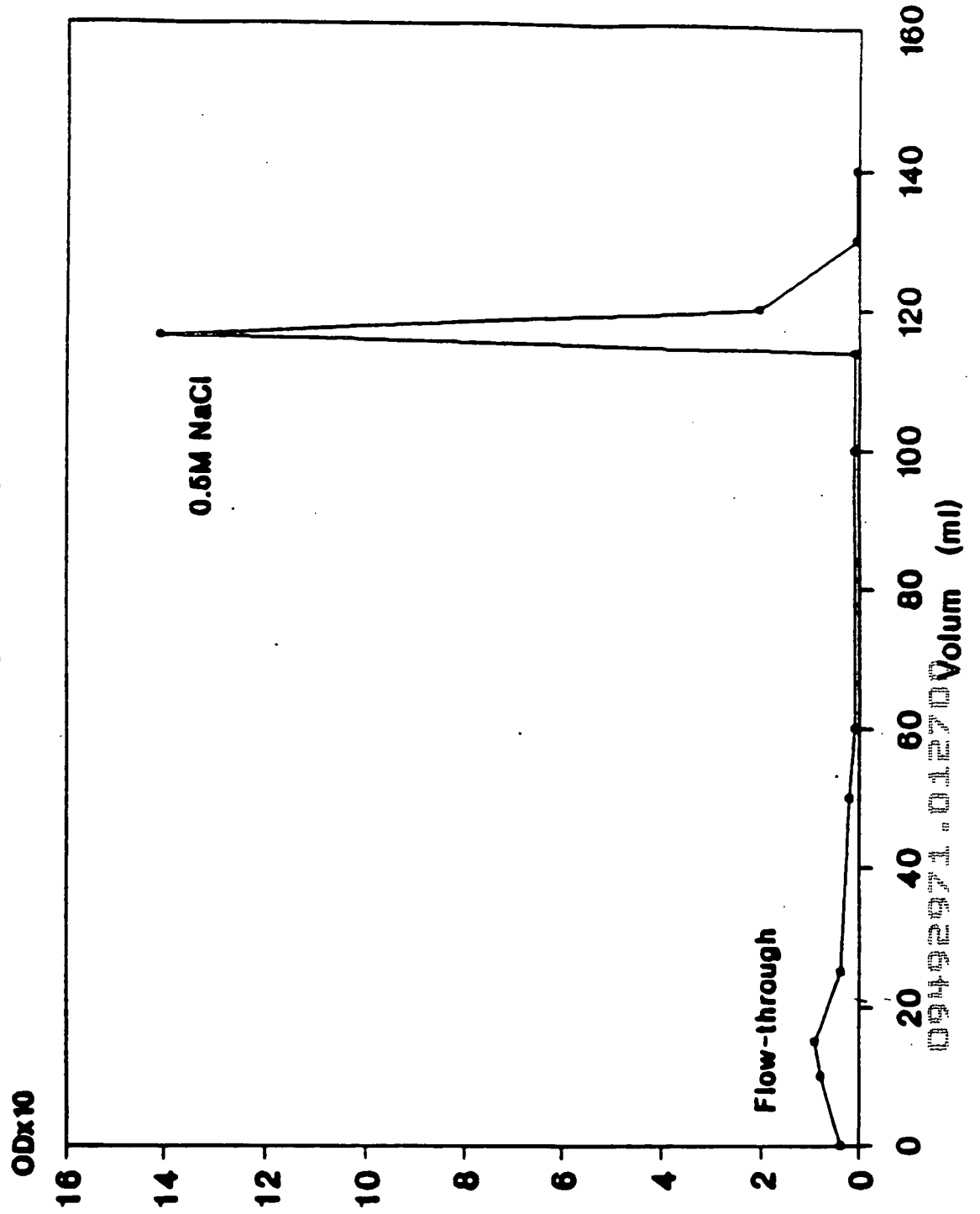


Figure 14

# 31kD / Q-Sepharose

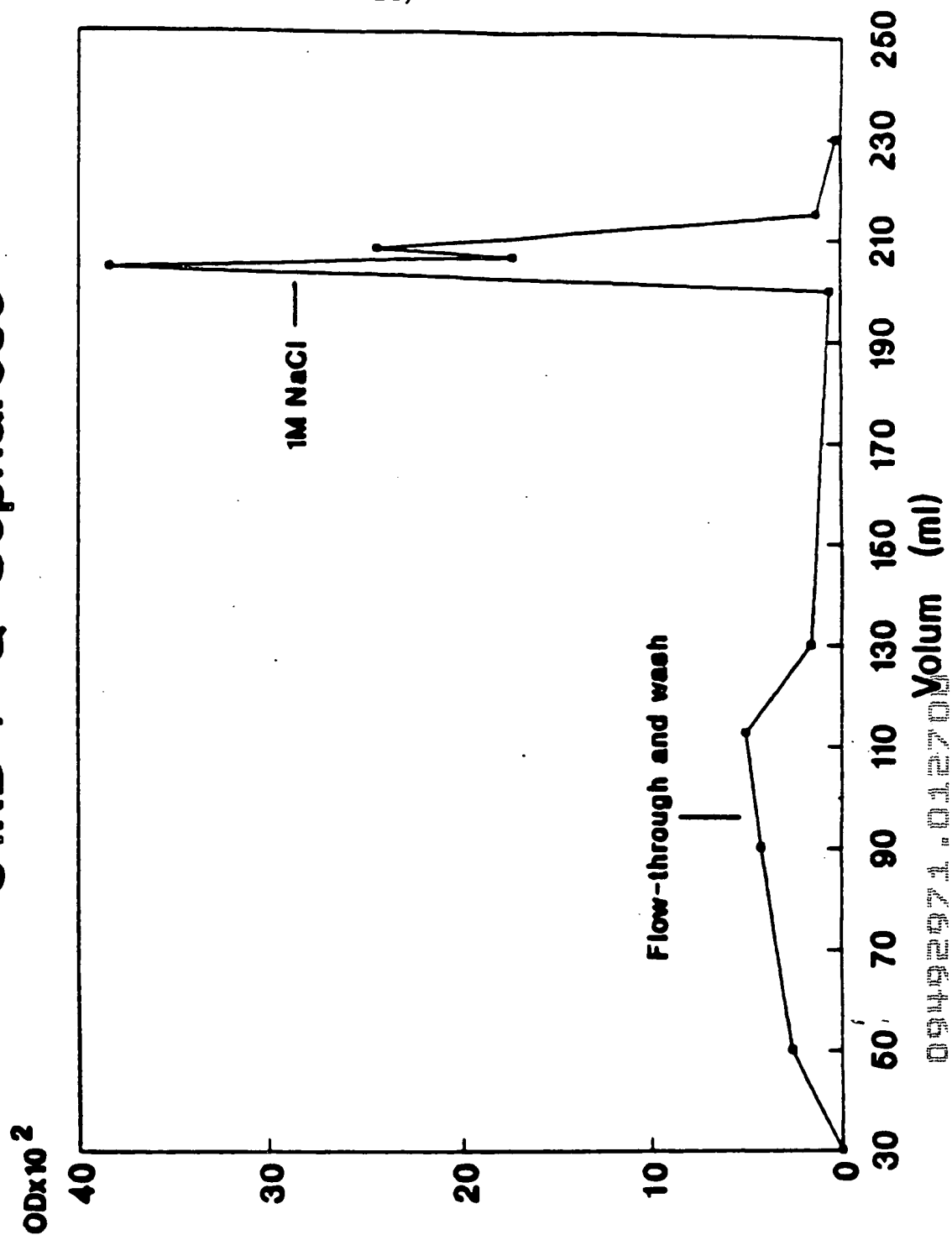
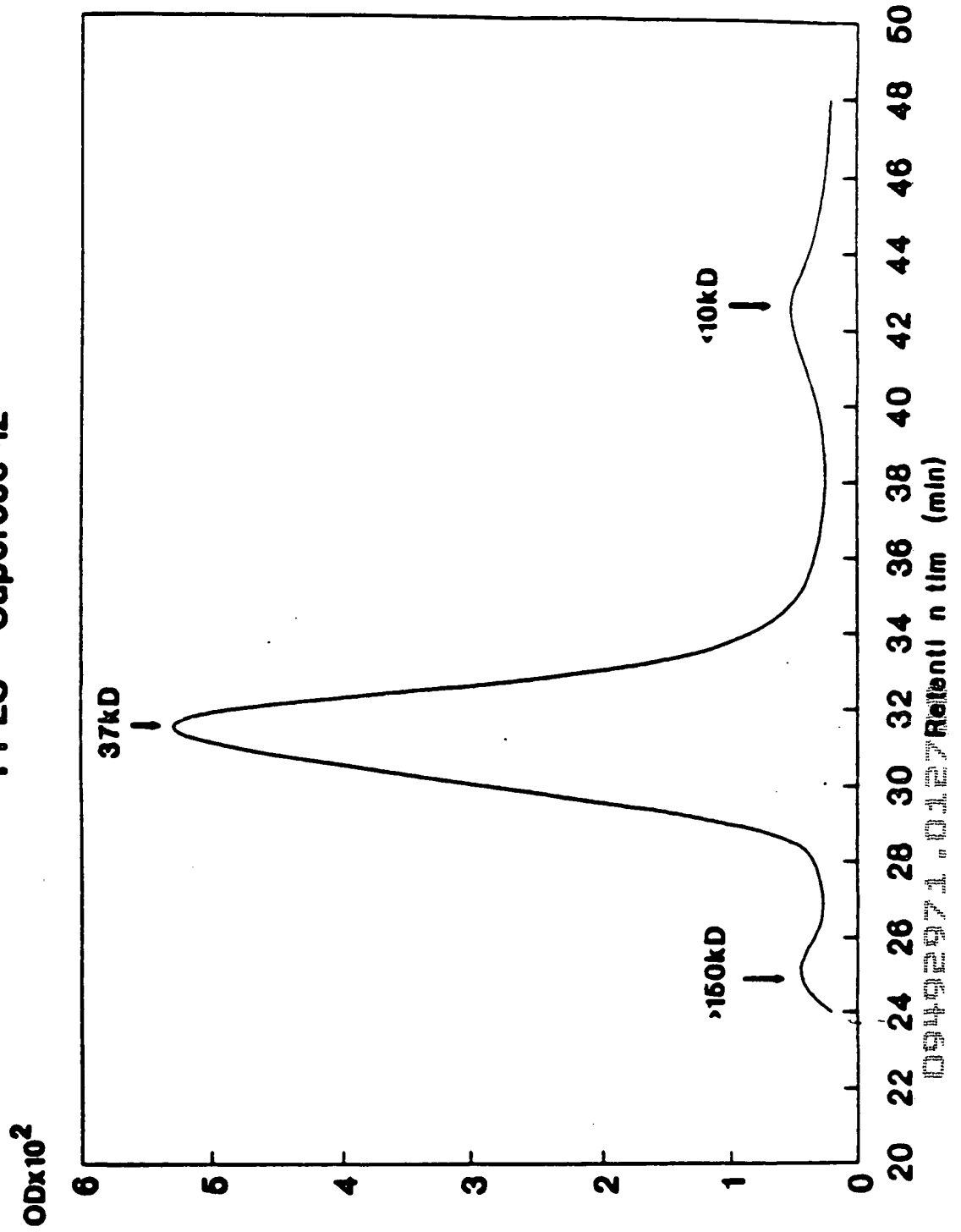


Figure 15

Mixture of rec. and plasmatic "31kD" FBD  
FPLC - Superose 12



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Figure 16

Pharmacokinetic Behavior of Fibronectin  
and Recombinant 31kD FBD in the Rat

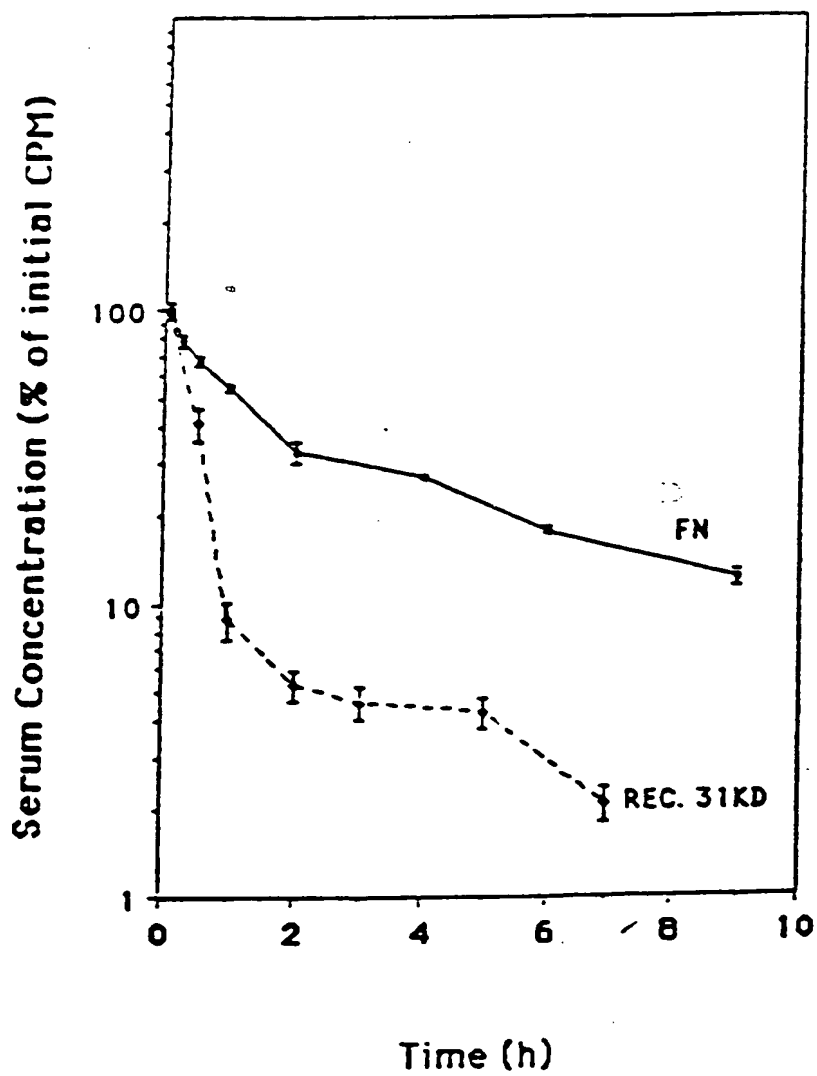


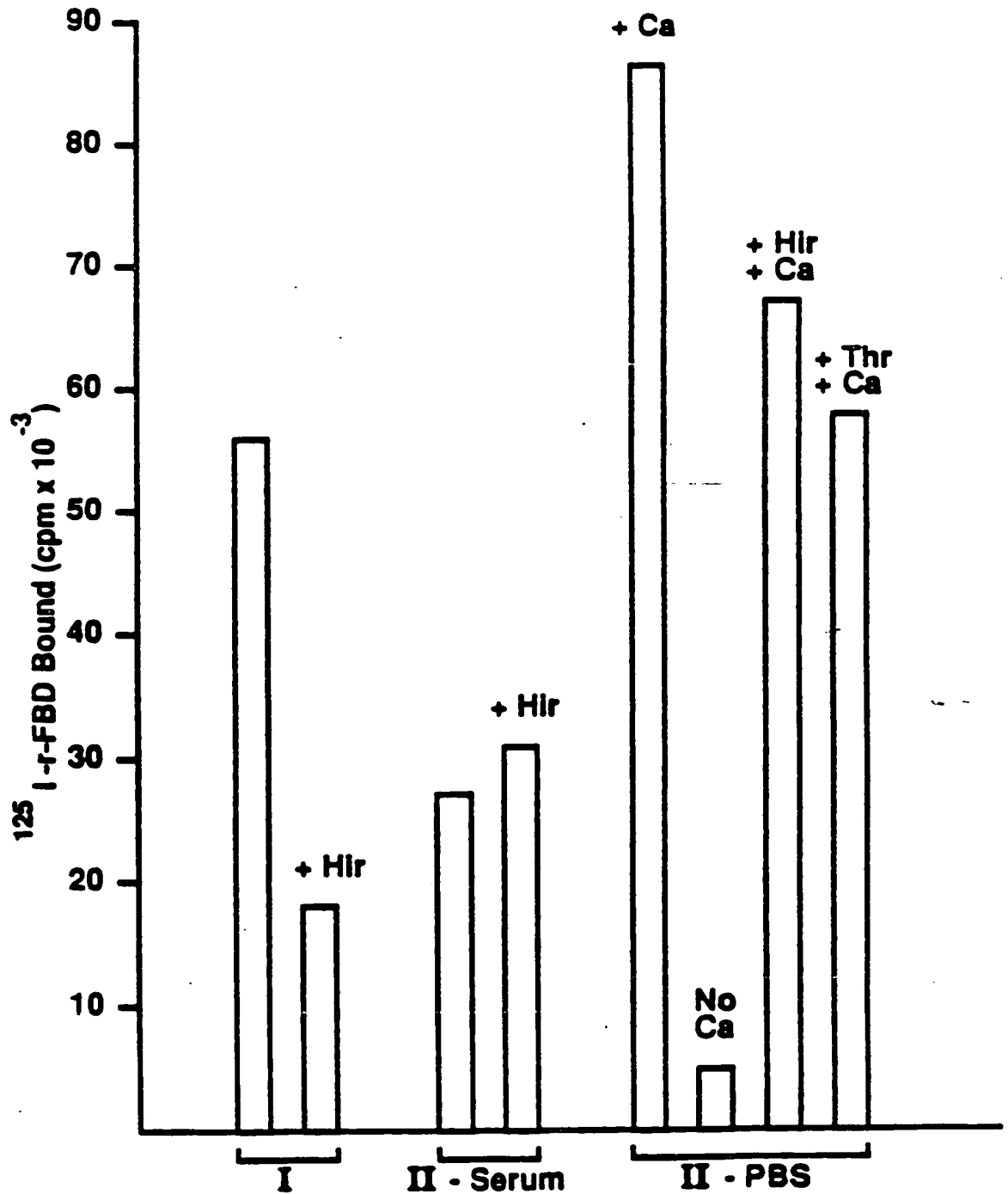


Figure 17

Binding of  $^{125}\text{I}$ -FBD to Fibrin;  
Effect of Thrombin and  $\text{Ca}^{++}$  ions.

I = Binding while clot formation

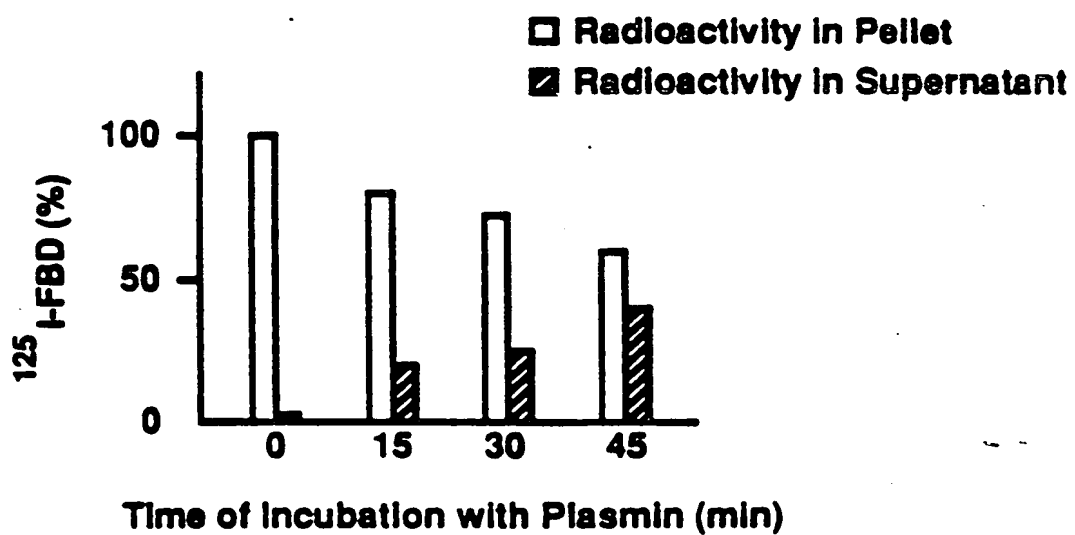
II = Binding to preformed Fibrin clot



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Figure 18

Release of  $^{125}$ I-FBD from Fibrin Clot by Plasmin.



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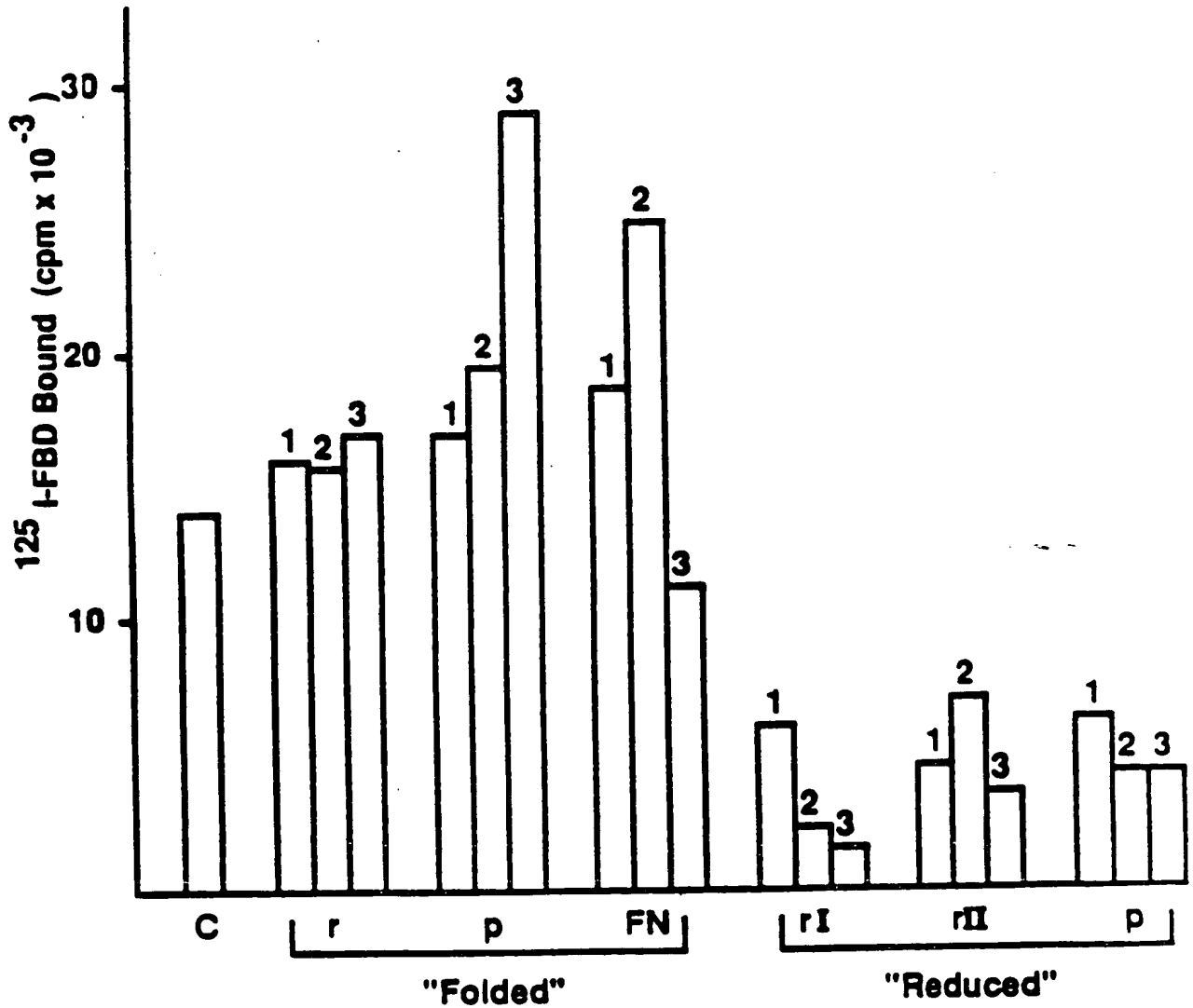
Figure 19

Binding of  $^{125}\text{I}$ -FBD during clot formation (Reaction I) ;  
Effect of unlabelled FBD and related molecules.

1 - 0.3  $\mu\text{M}$  Unlabelled competitors

2 - 1.0  $\mu\text{M}$  " "

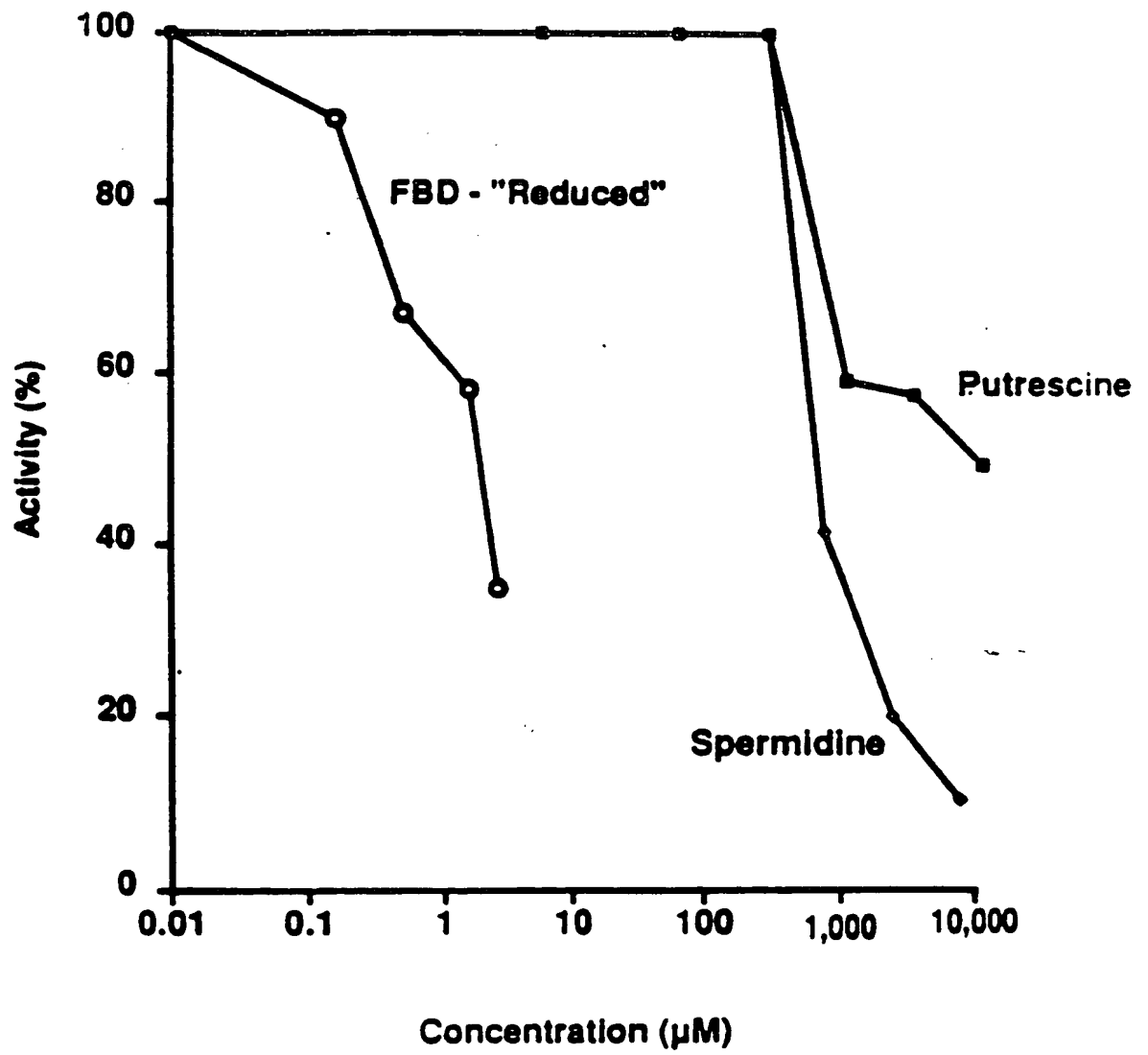
3 - 3.0  $\mu\text{M}$  " "



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Figure 20

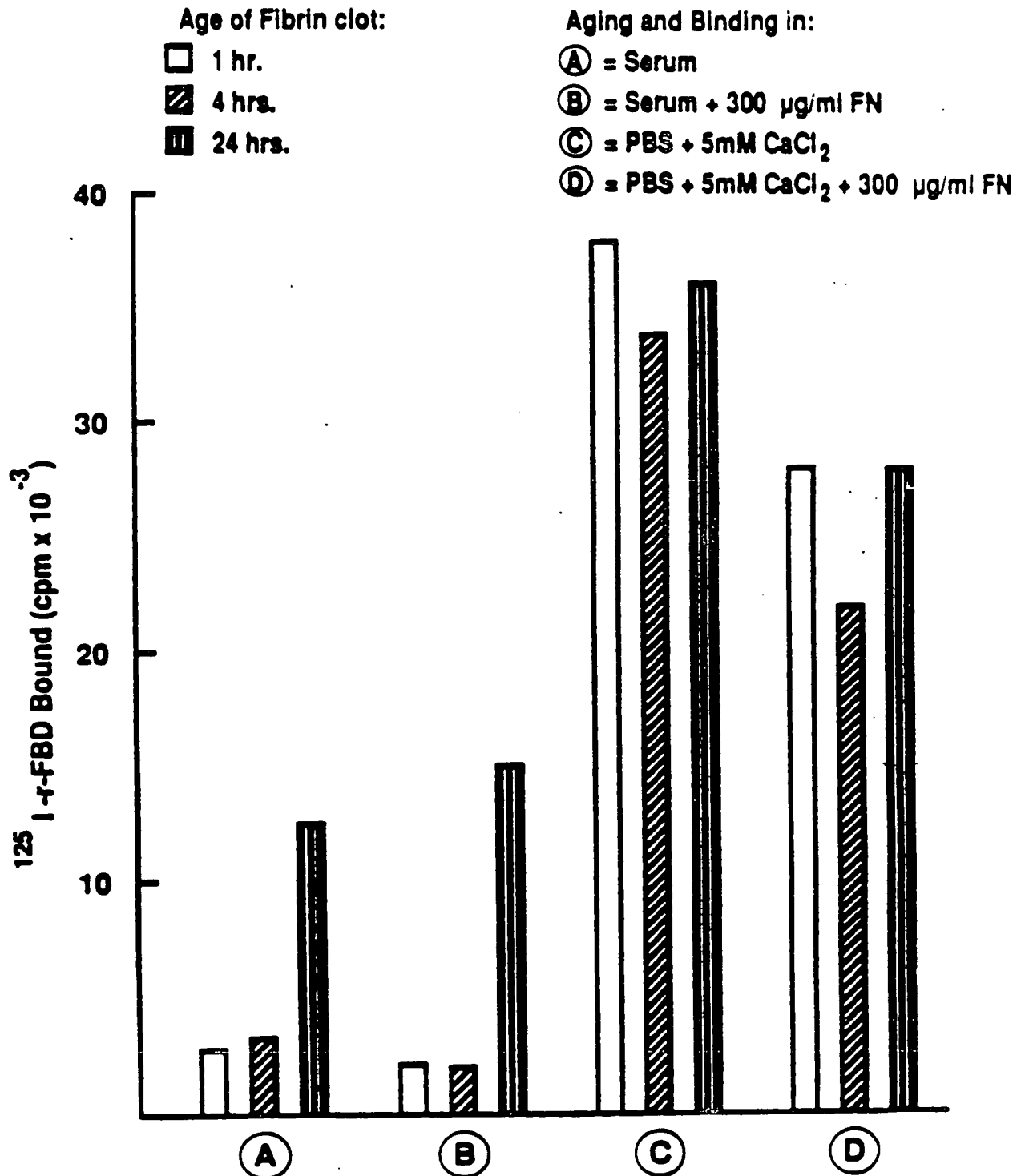
Binding of  $^{125}$ I-FBD to Fibrin ( Reaction II );  
Effect of Transglutaminase Inhibitors.



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Figure 21

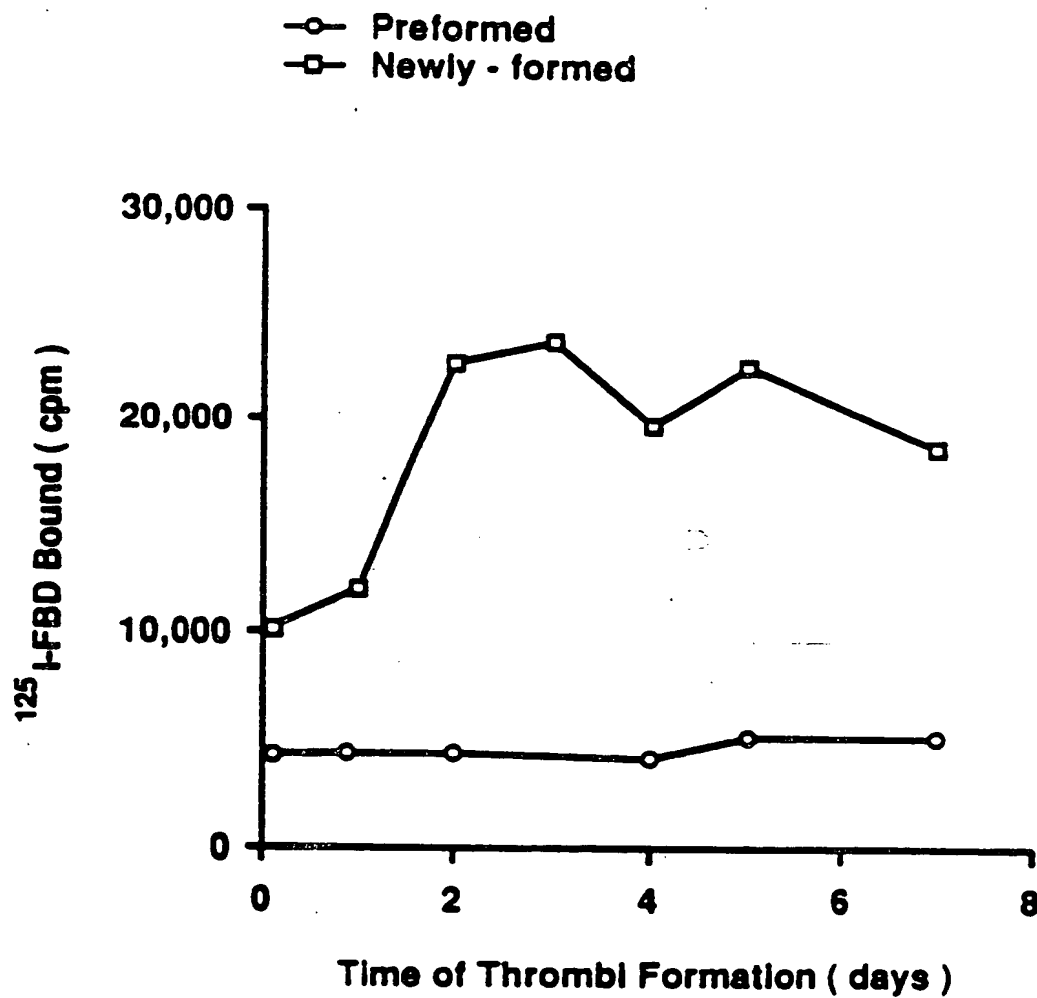
Binding of  $^{125}\text{I}$ -FBD to preformed Fibrin clot (Reaction II);  
Effect of Fibrin clot Age on the Binding (aging at 37° C).



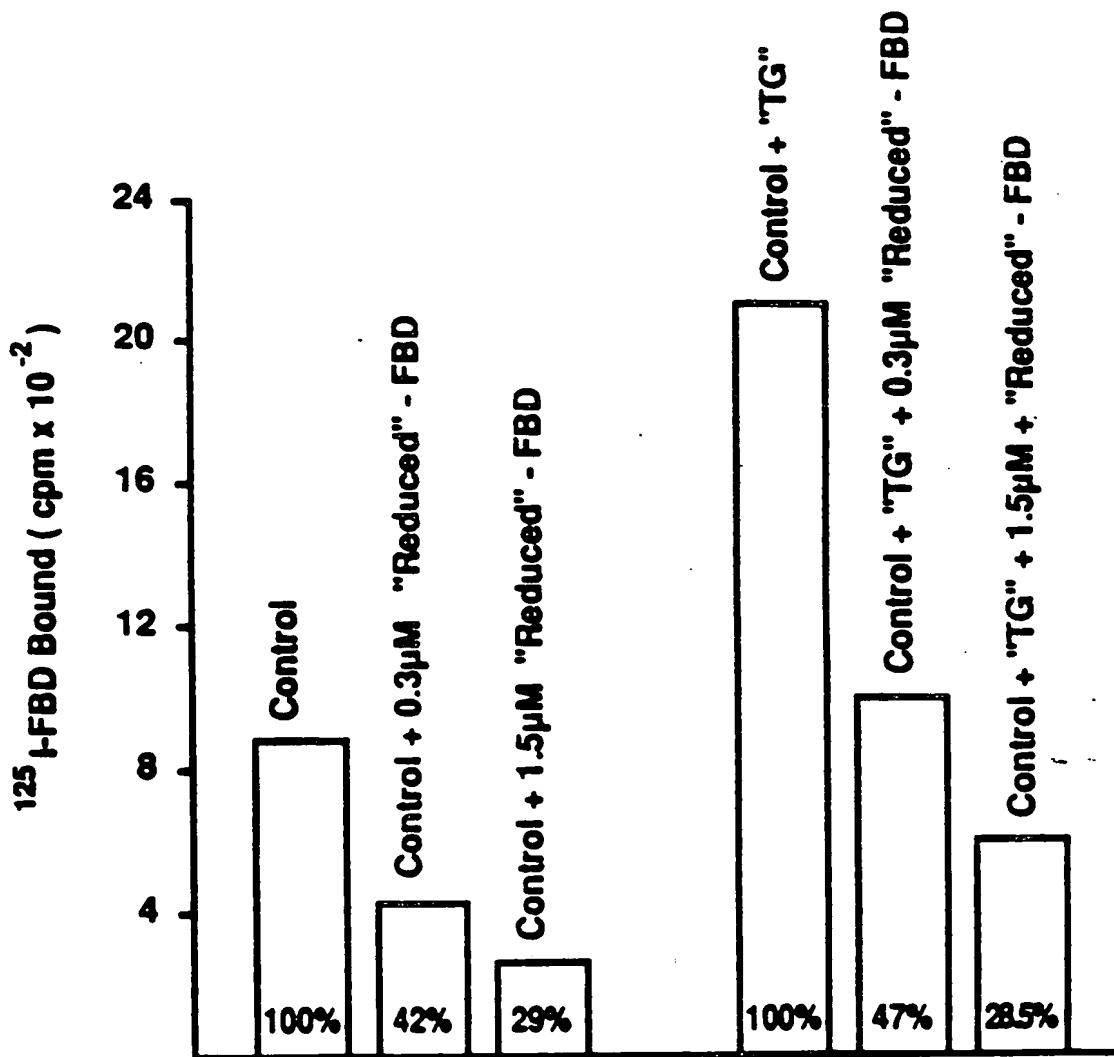
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Figure 22

### Binding of FBD to "Naive" Thrombi



# Binding of FBD to Fibrin ( Reaction I ); Effect of Transglutaminase ("TG") and "Reduced" - FBD



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Figure 24

Binding of  $^{125}\text{I}$ -FBD to ECM,  
Effect of Ligand Concentration and Thrombin

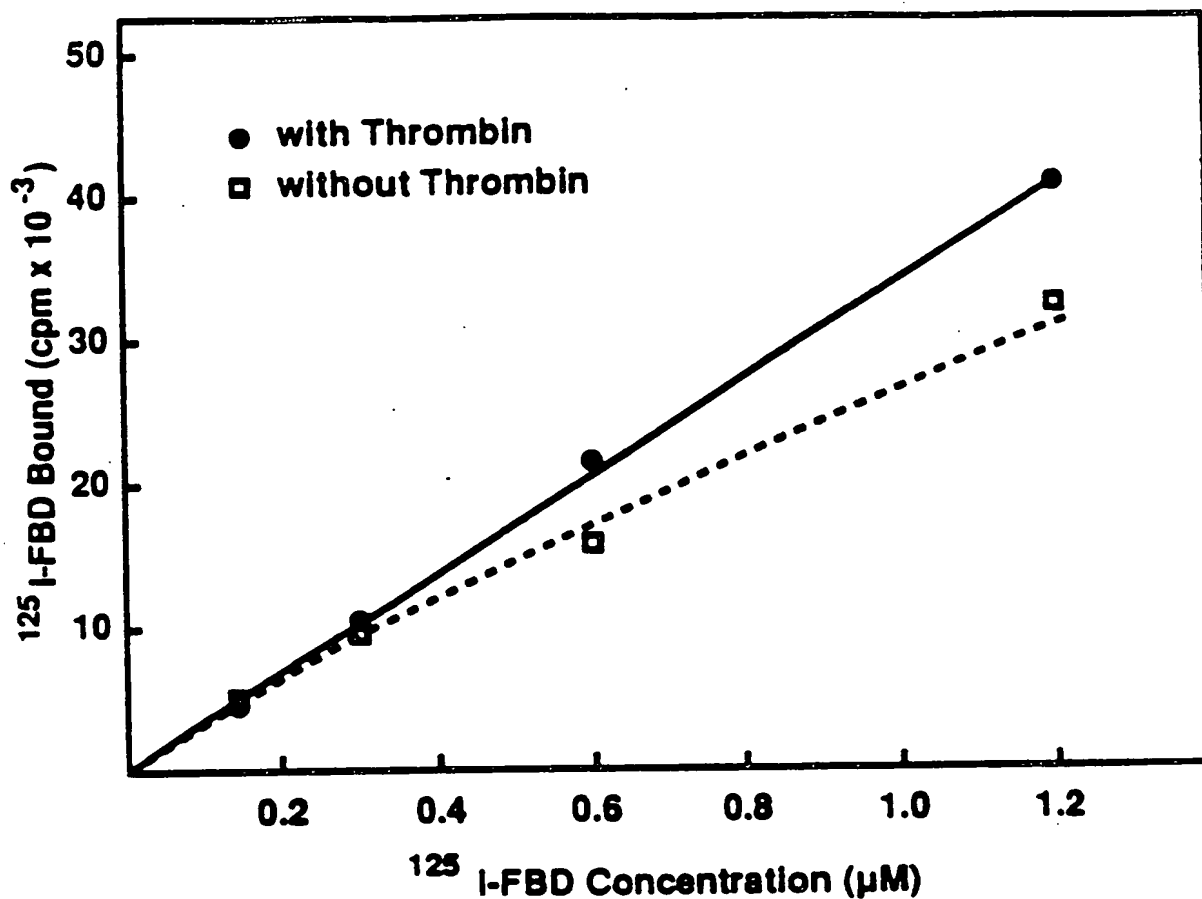
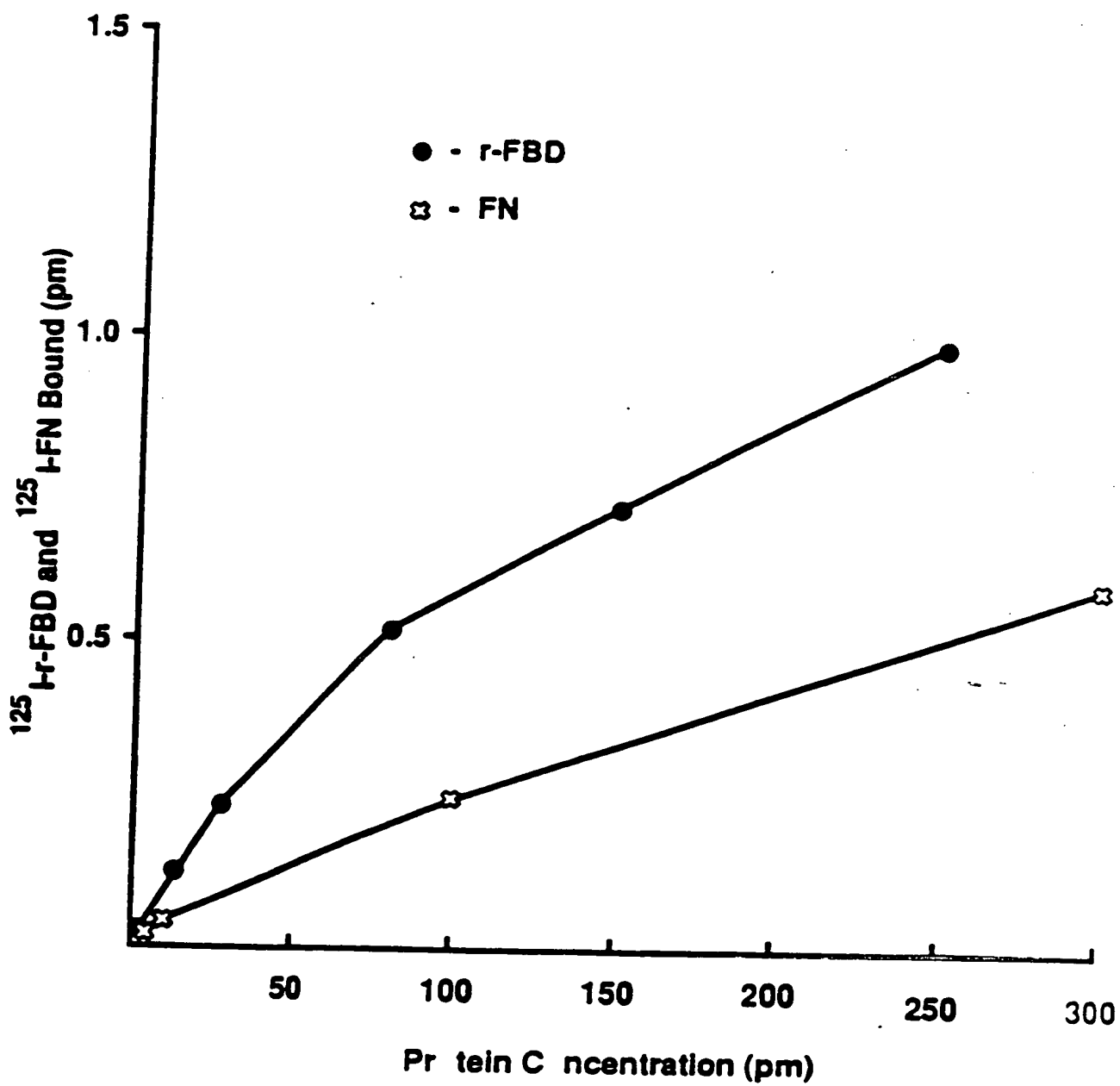




Figure 25

Binding of  $^{125}\text{I}$ - ( FN, r-FBD ) to *S. aureus*



Figur 26

Binding of  $^{125}\text{I}$ -FBD to *S. aureus*;  
Competition with "Folded" and "Reduced" forms.

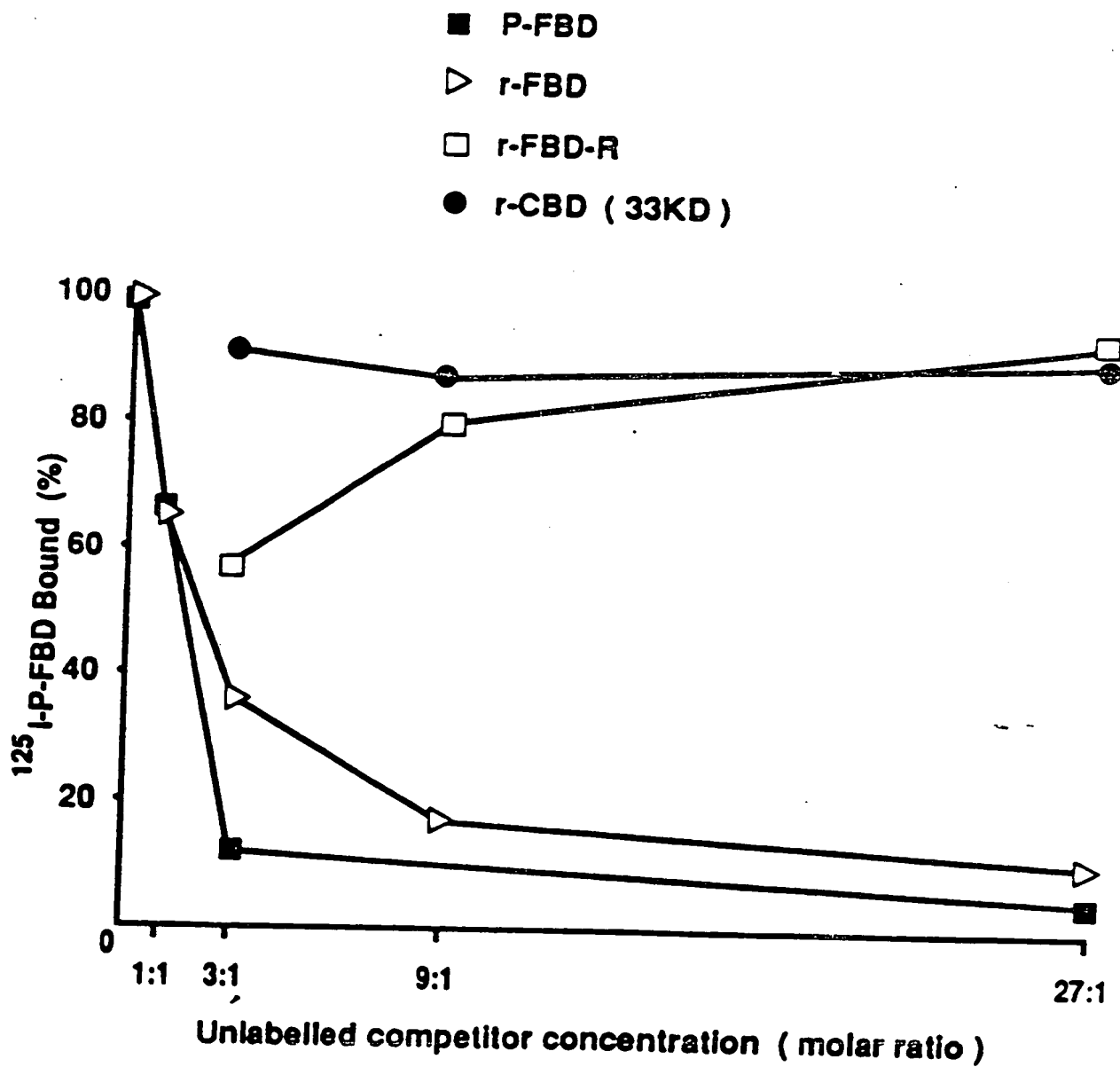


Figure 27

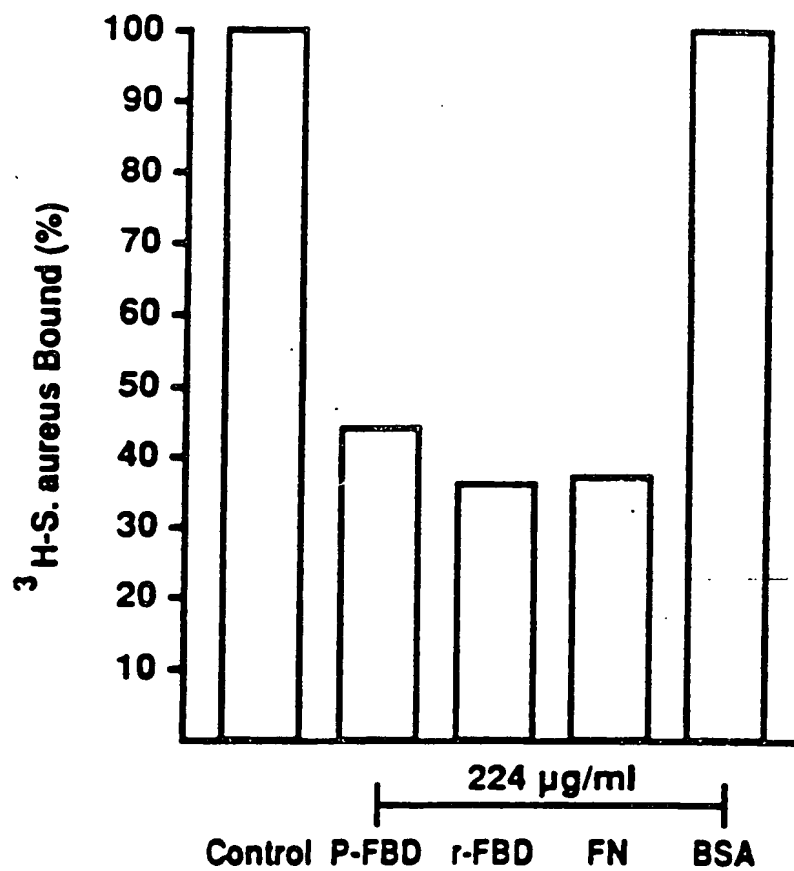
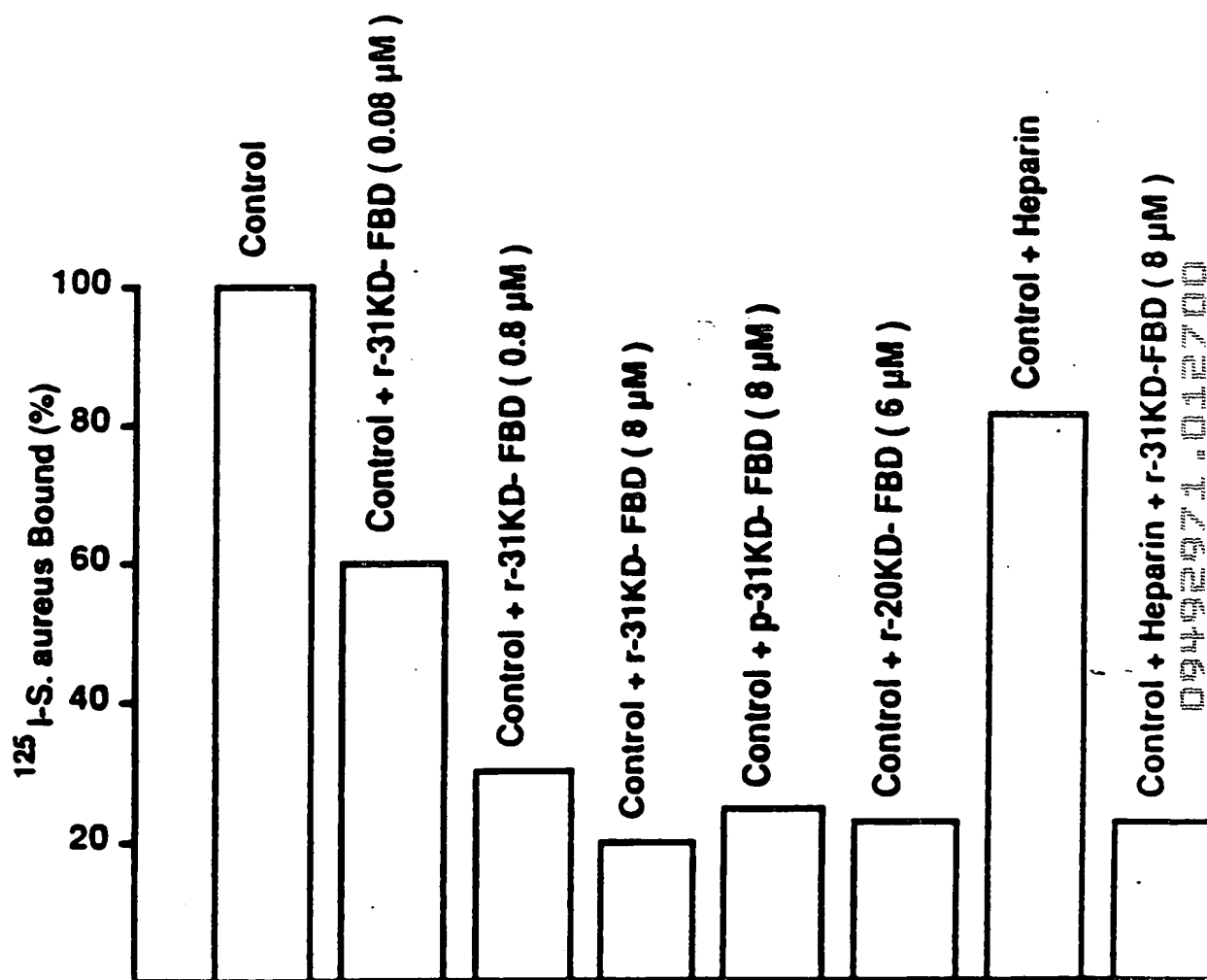
Binding of *S. aureus* to Immobilized FN.

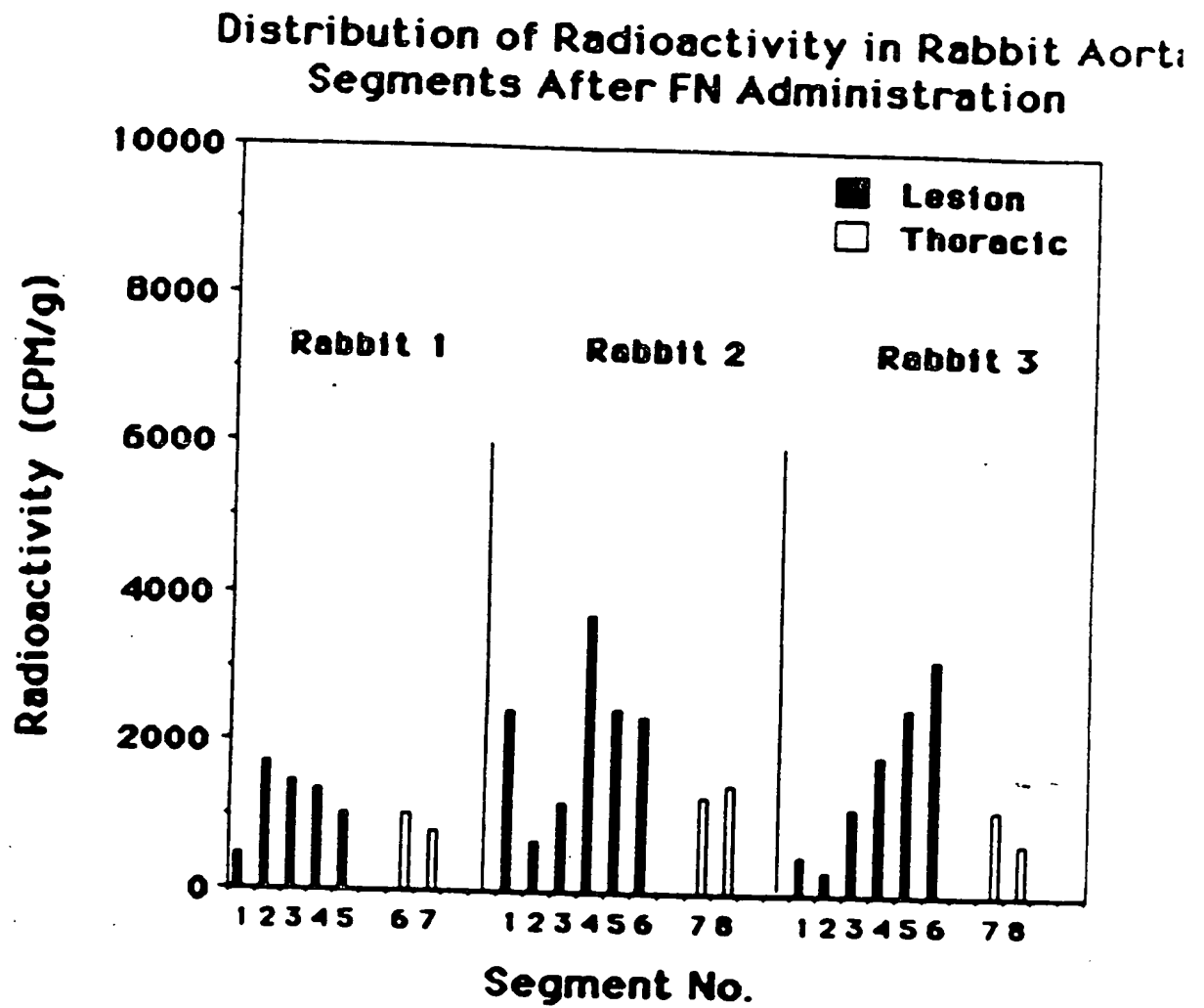
Figure 28

Binding of *S. aureus* to Bronchial Catheters;  
Effect of FBD and Heparin.



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Figure 29A

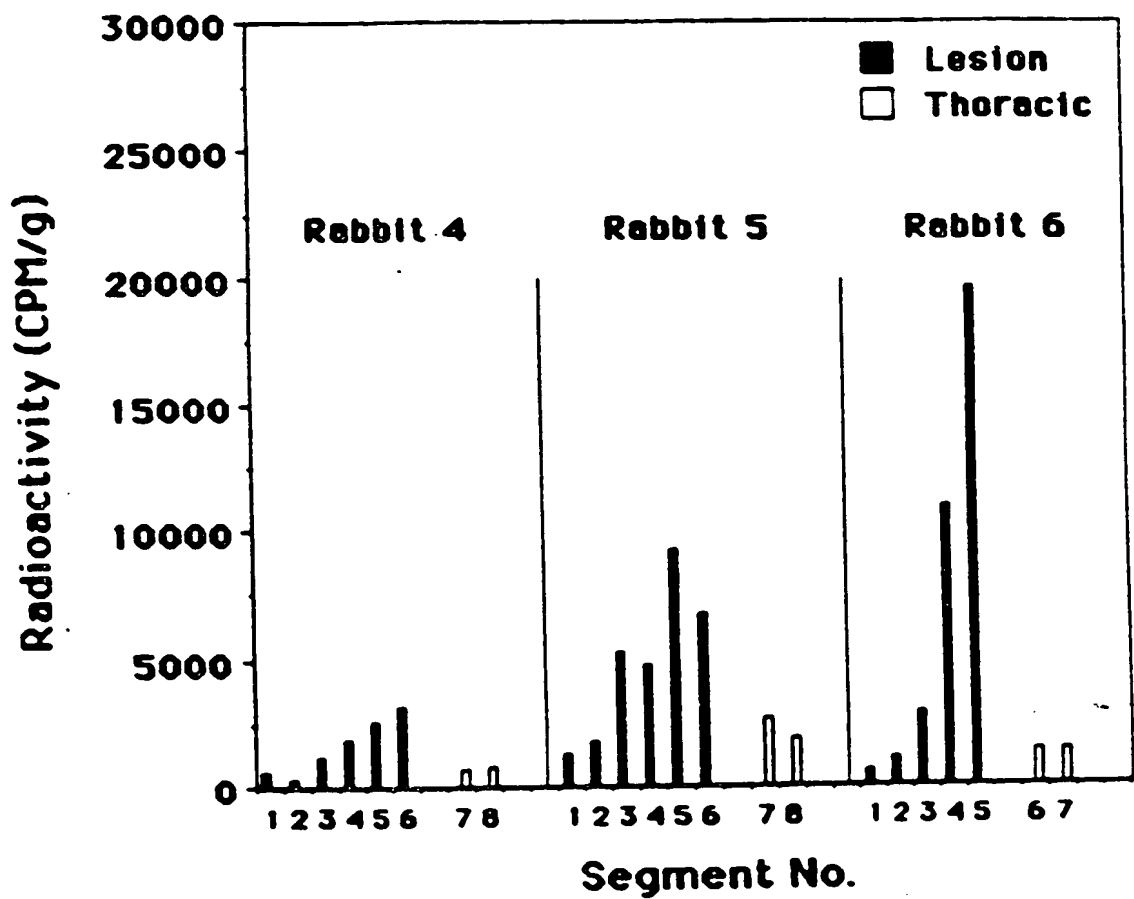


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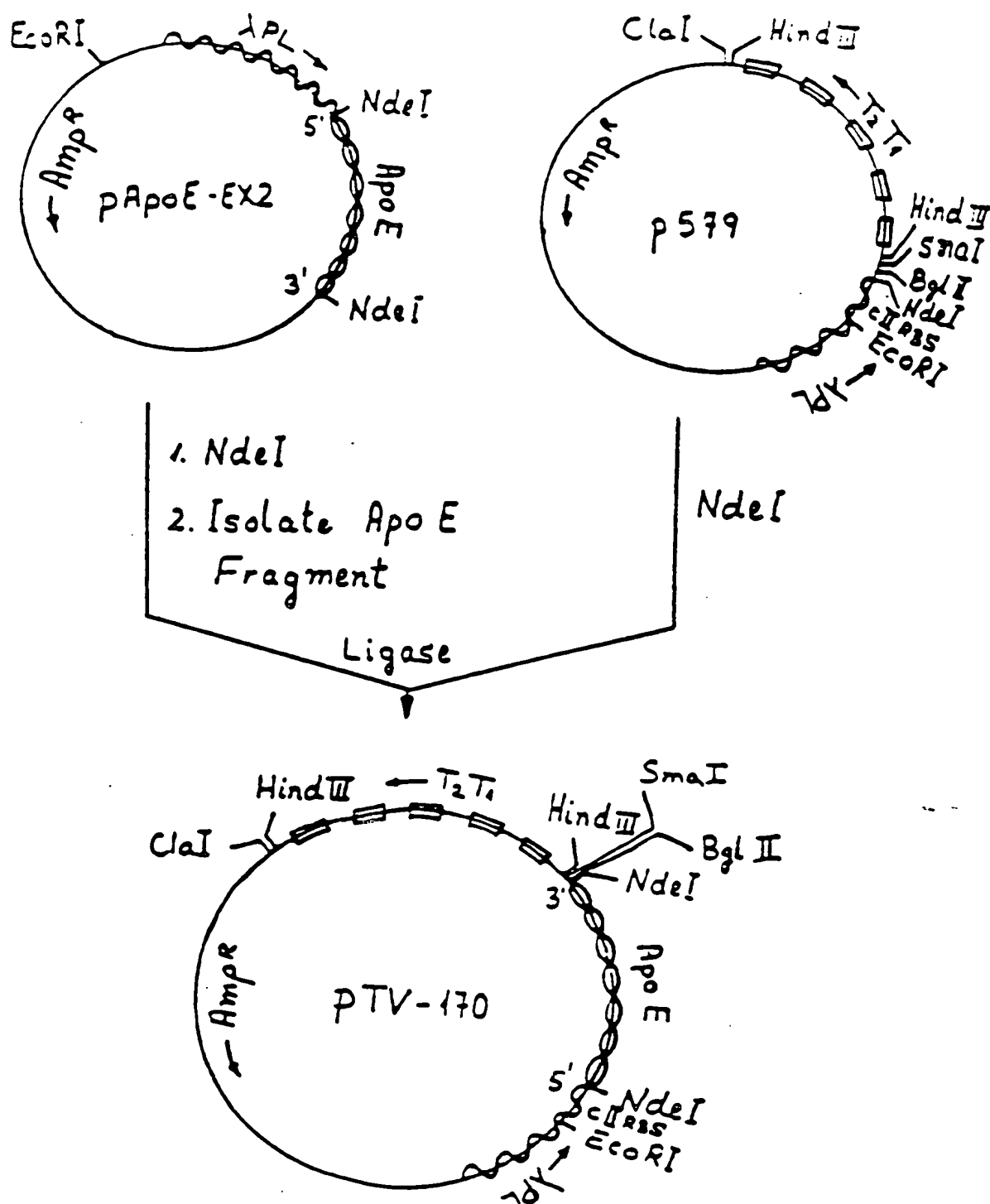
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Figure 29B

**Distribution of Radioactivity in Rabbit Aorta Segments After 31kD FBD Administration**

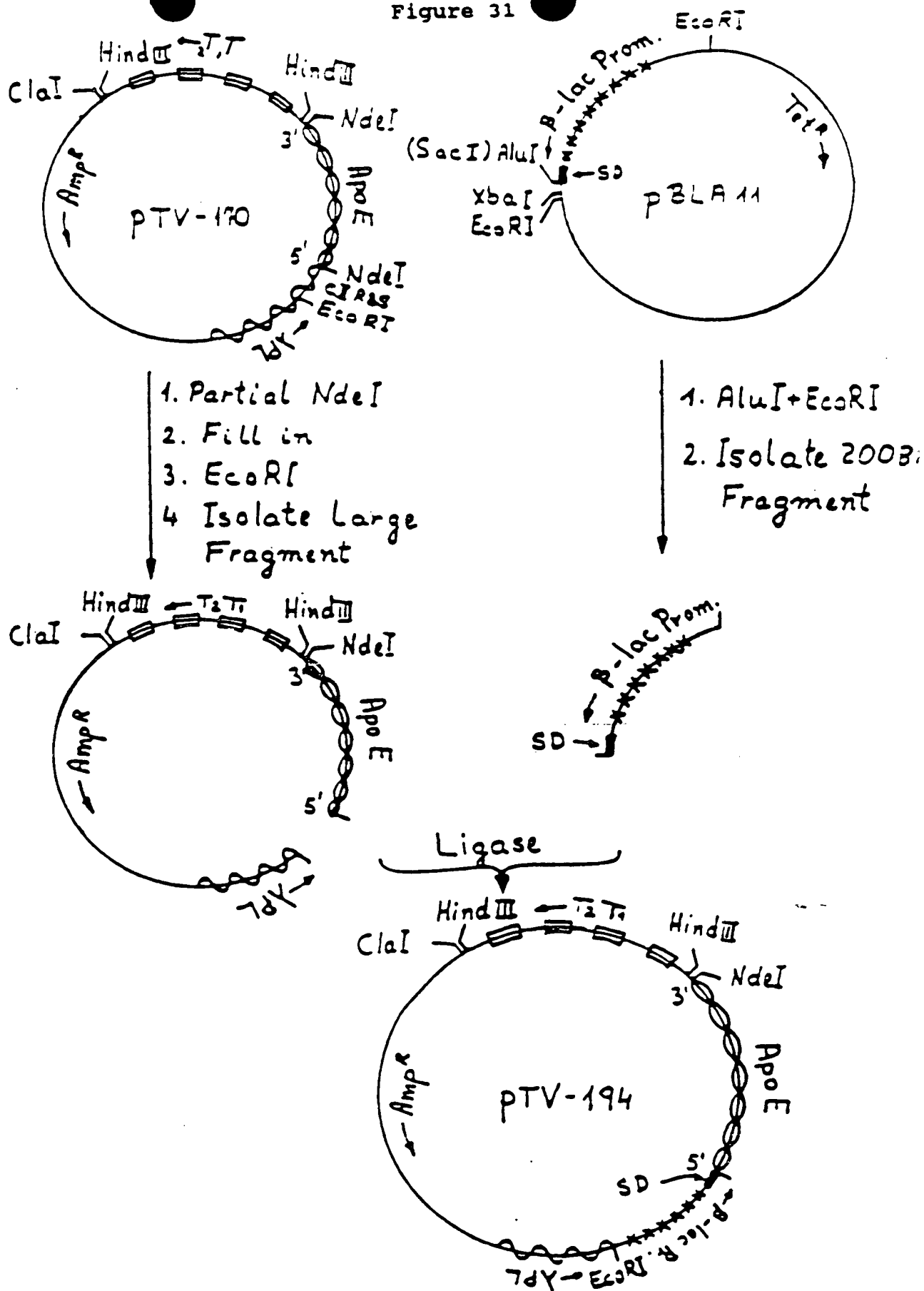


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Figure 30



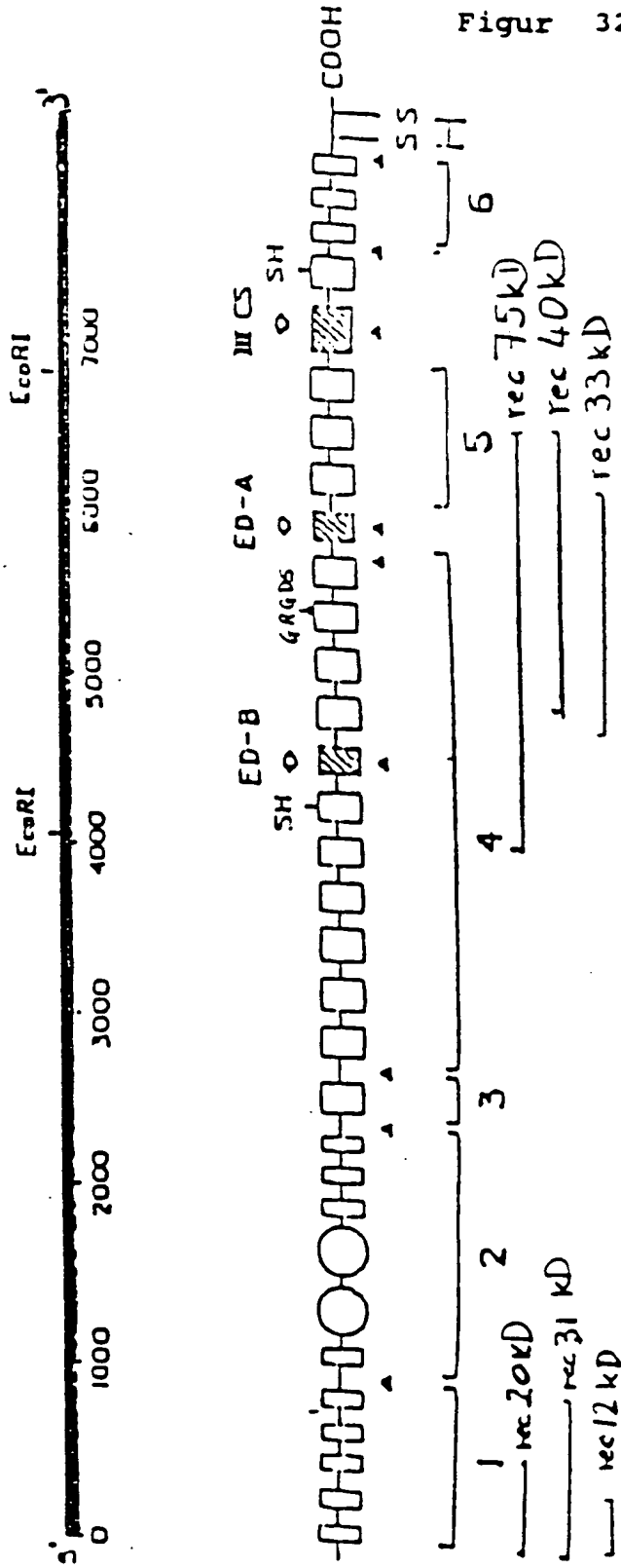
004492971.012700

Figure 31



09492971.012700





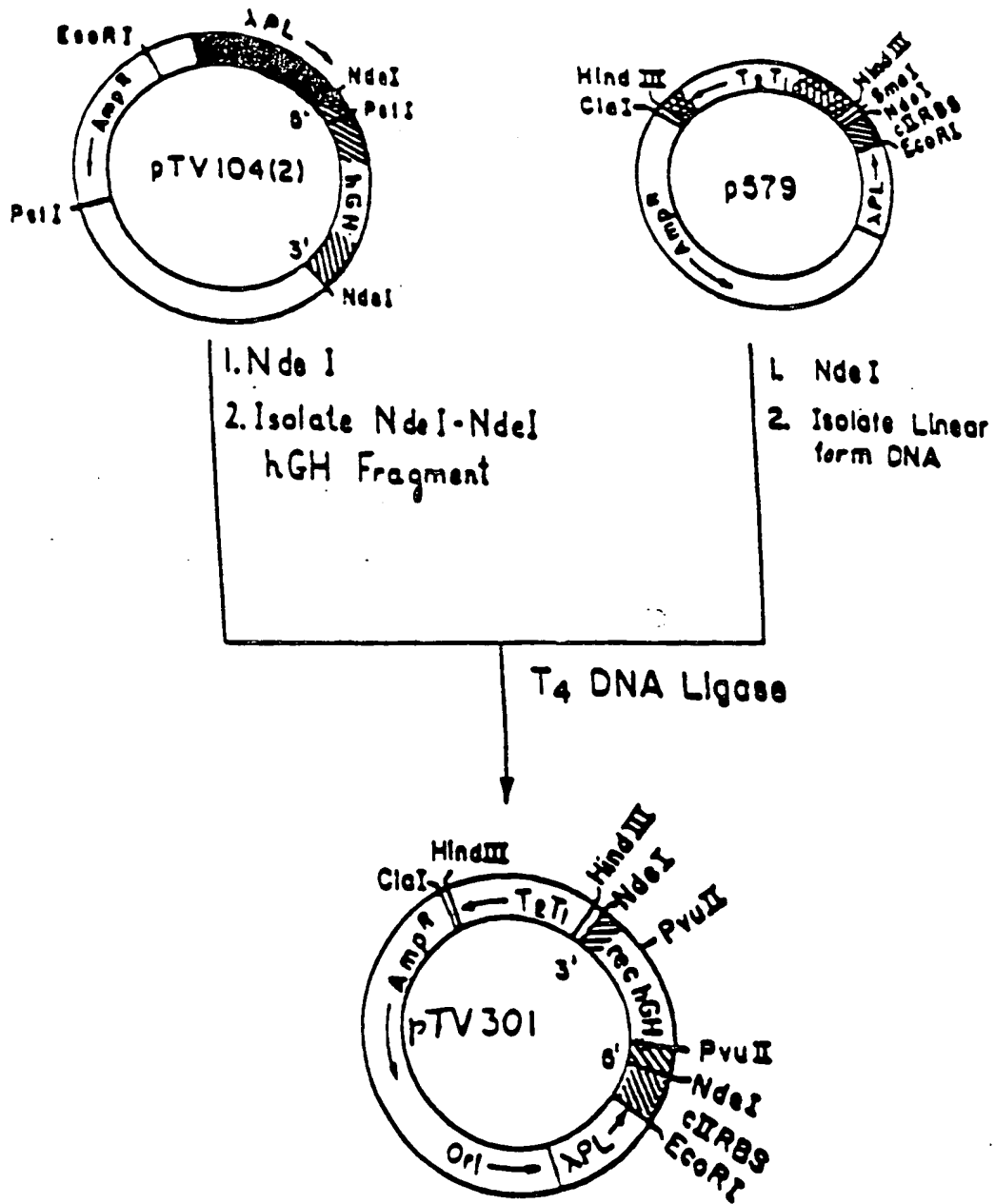
HEPARIN	COLLAGEN	HEPARIN [DNA]	CELL	HEPARIN [CELL]	FIBRIN
S. AUREUS					
FIBRIN					

## Nucleotides:

09492971-012700

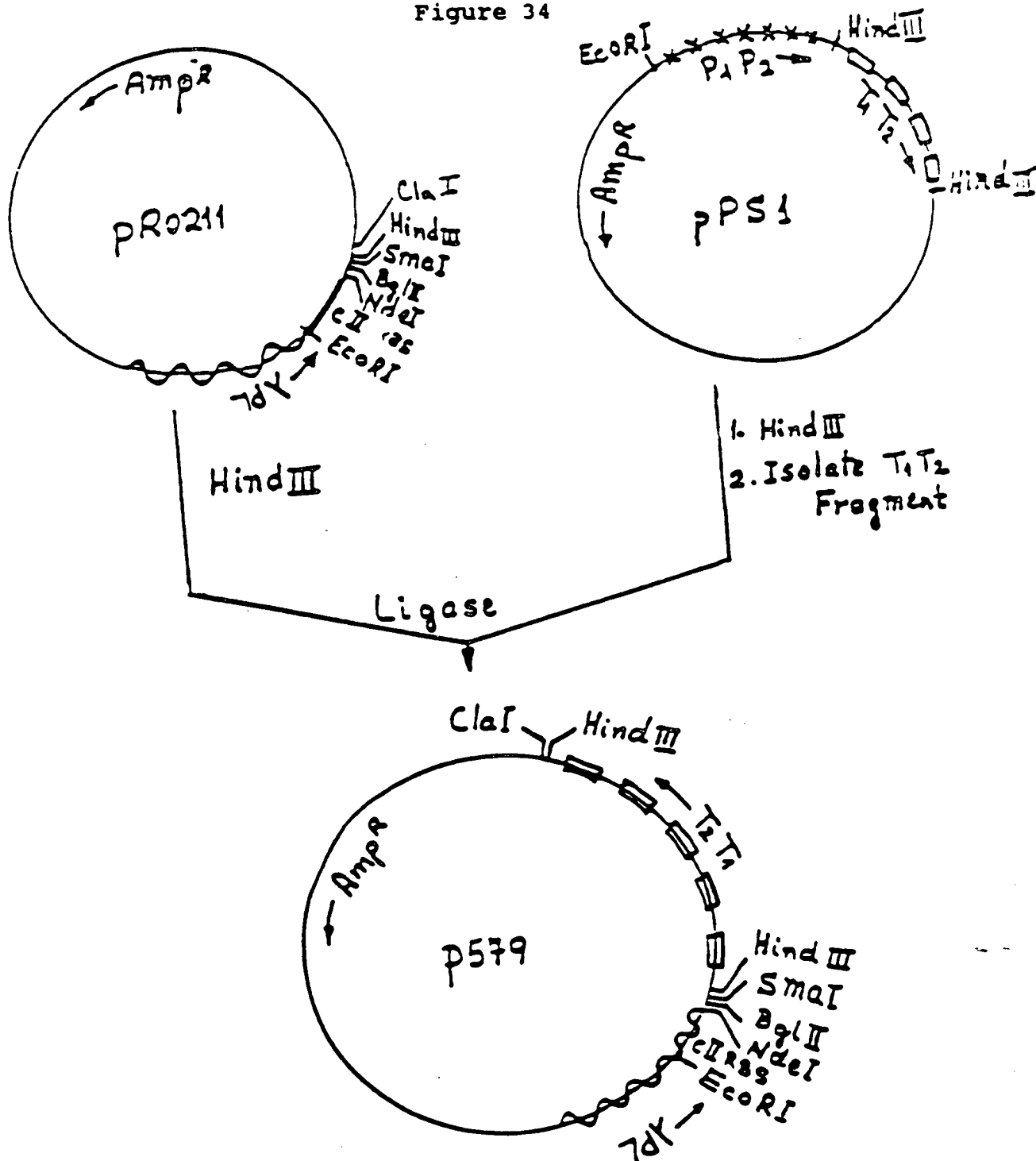
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Figur 33



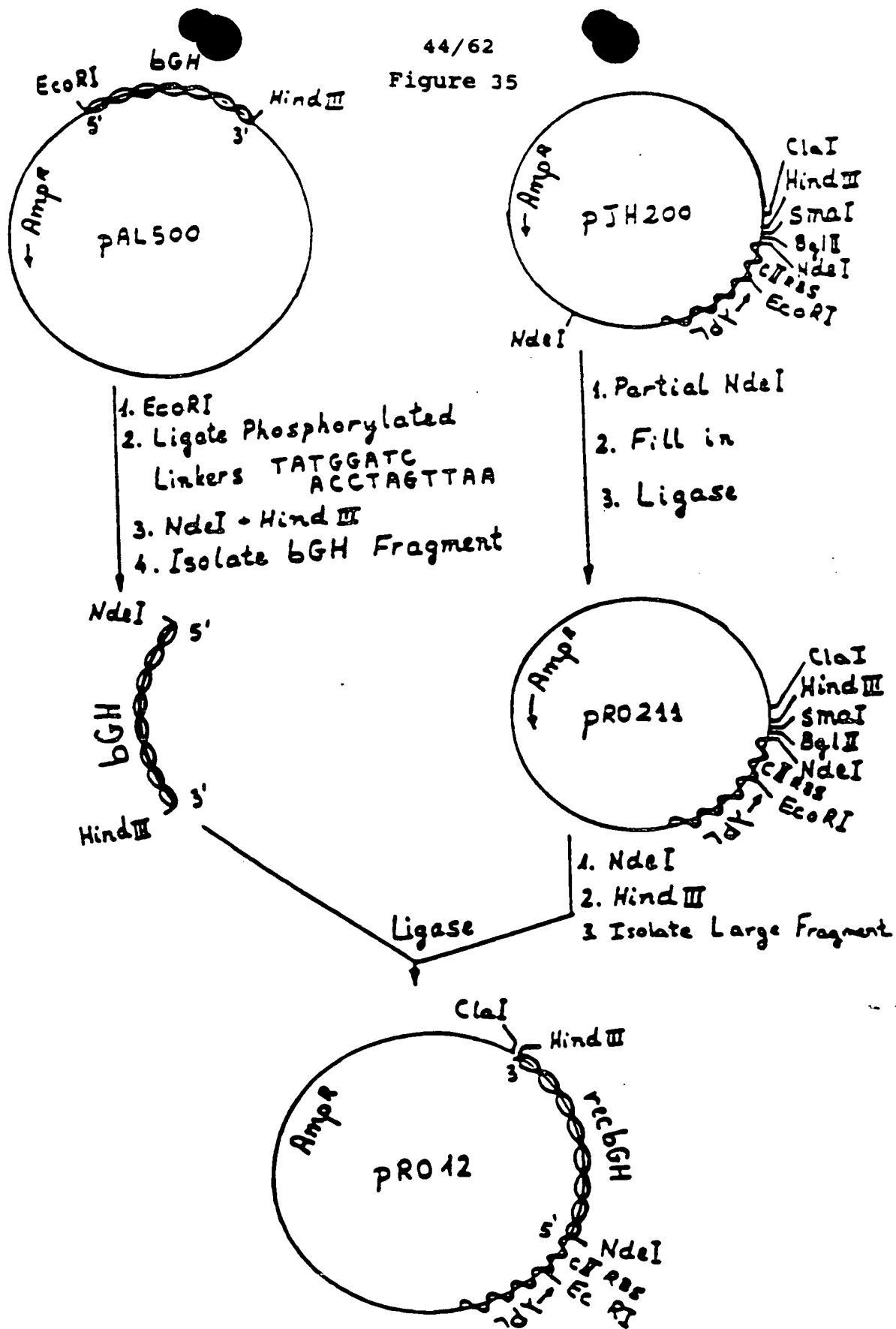
002270" T 2525460

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Figure 34



002270-1.02700

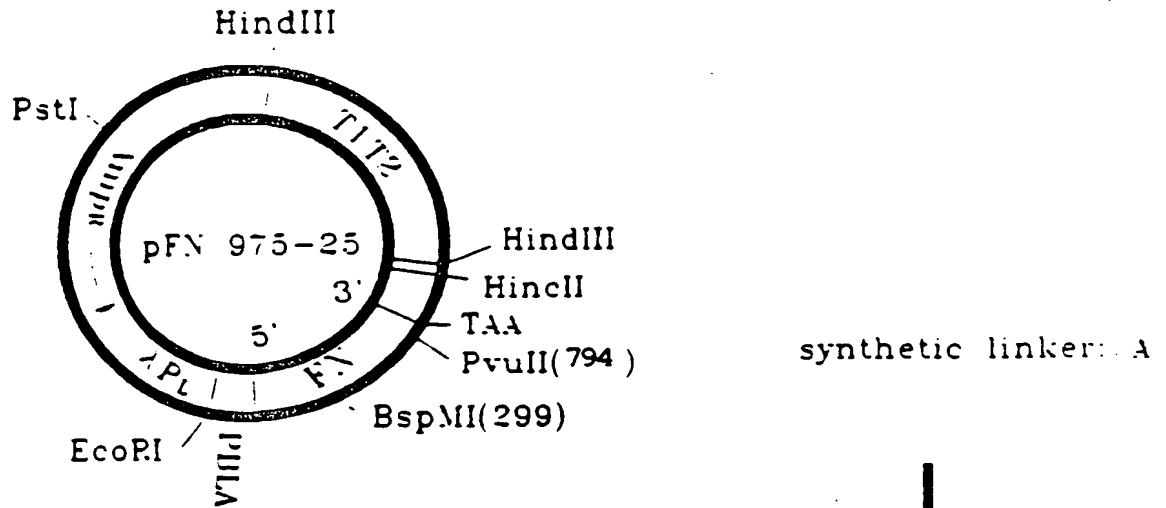
Figure 35



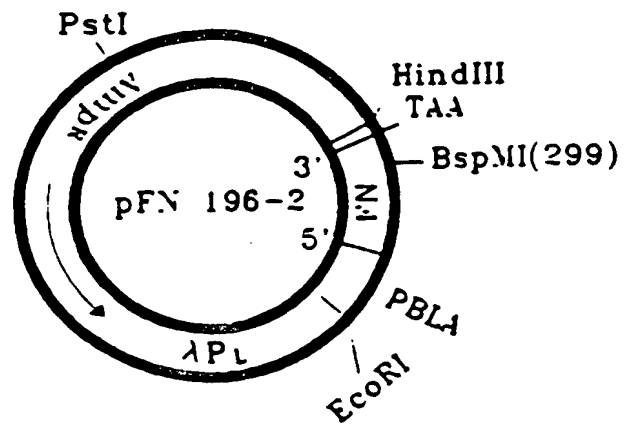
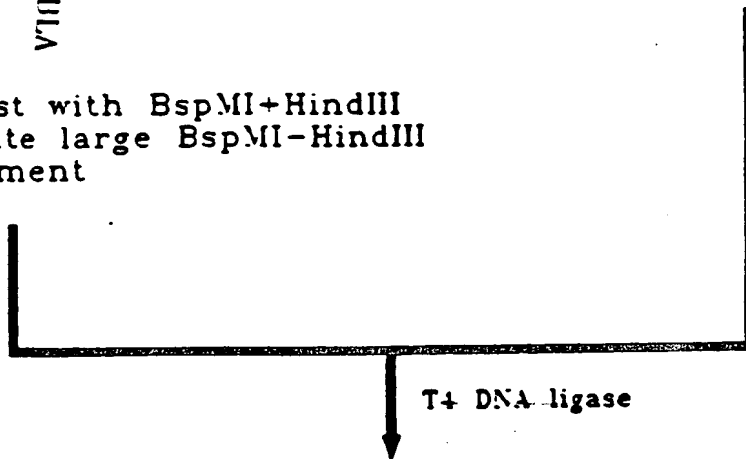
00492971.012700

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Figur 36



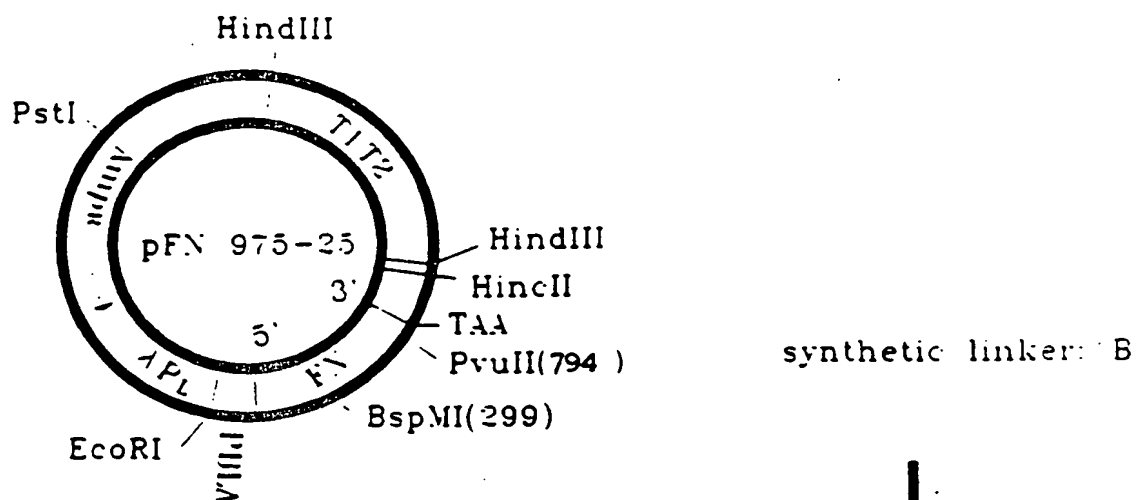
1. digest with BspMI+HindIII
2. isolate large BspMI-HindIII fragment



11/104-2

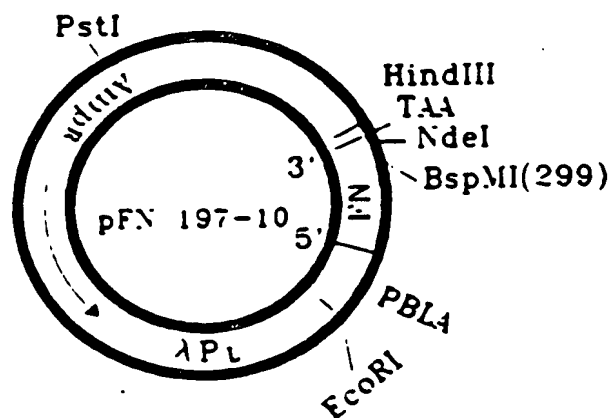
002270" T 2626460

Figure 37



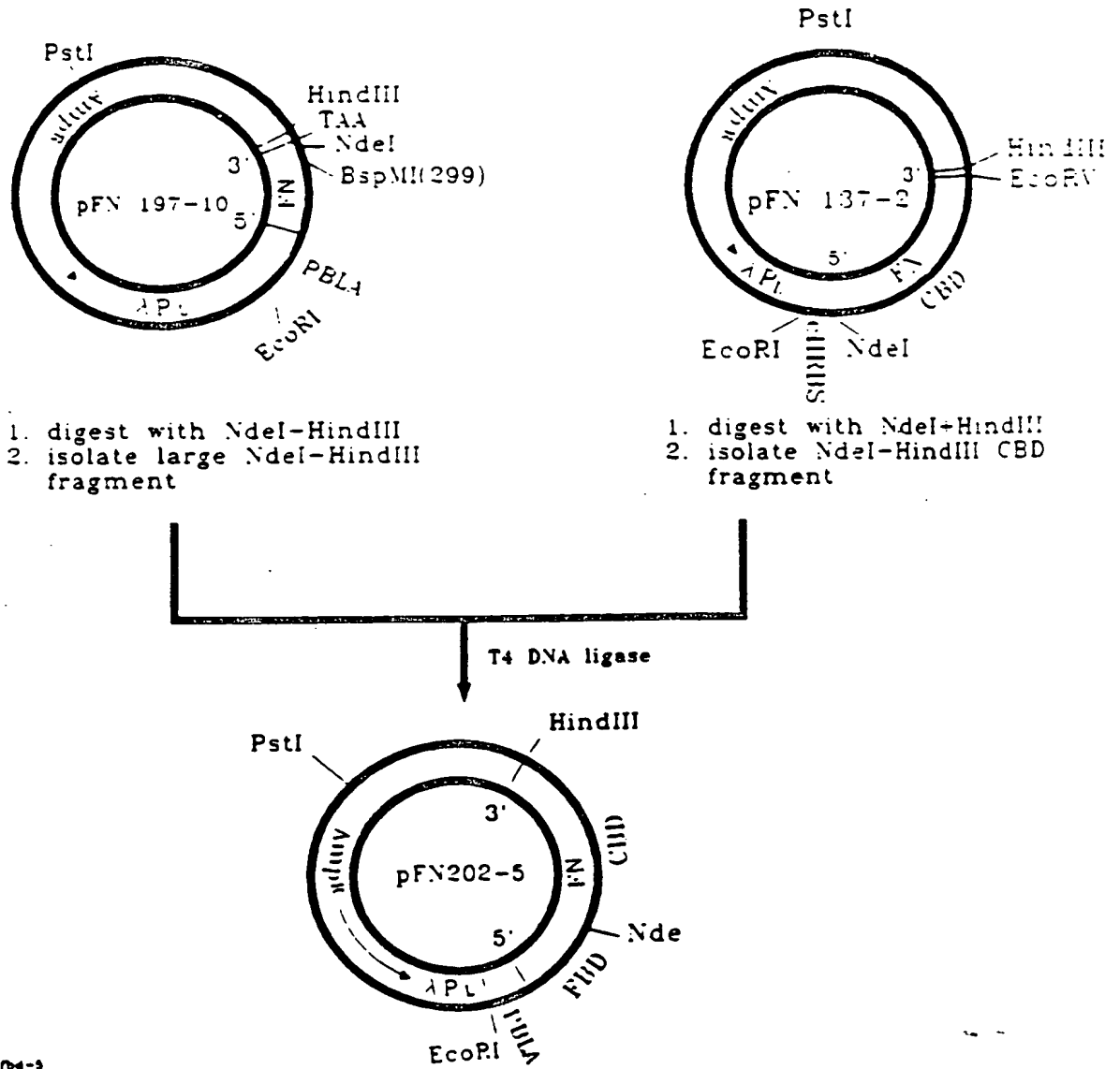
1. digest with BspMI+HindIII
2. isolate large BspMI-HindIII fragment

T4 DNA ligase



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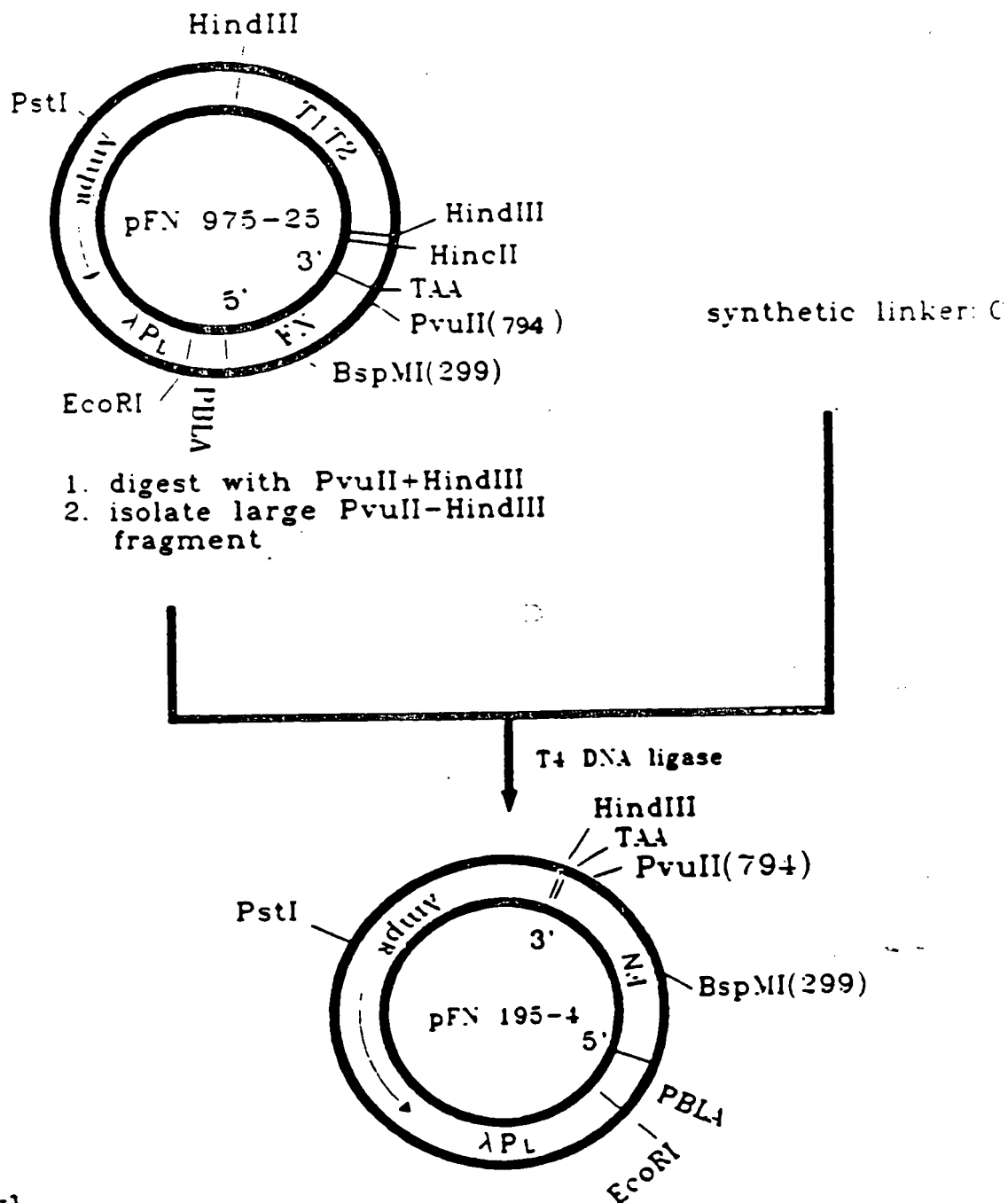
Figure 38



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002270-1-012700

Figure 39





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Figure 40

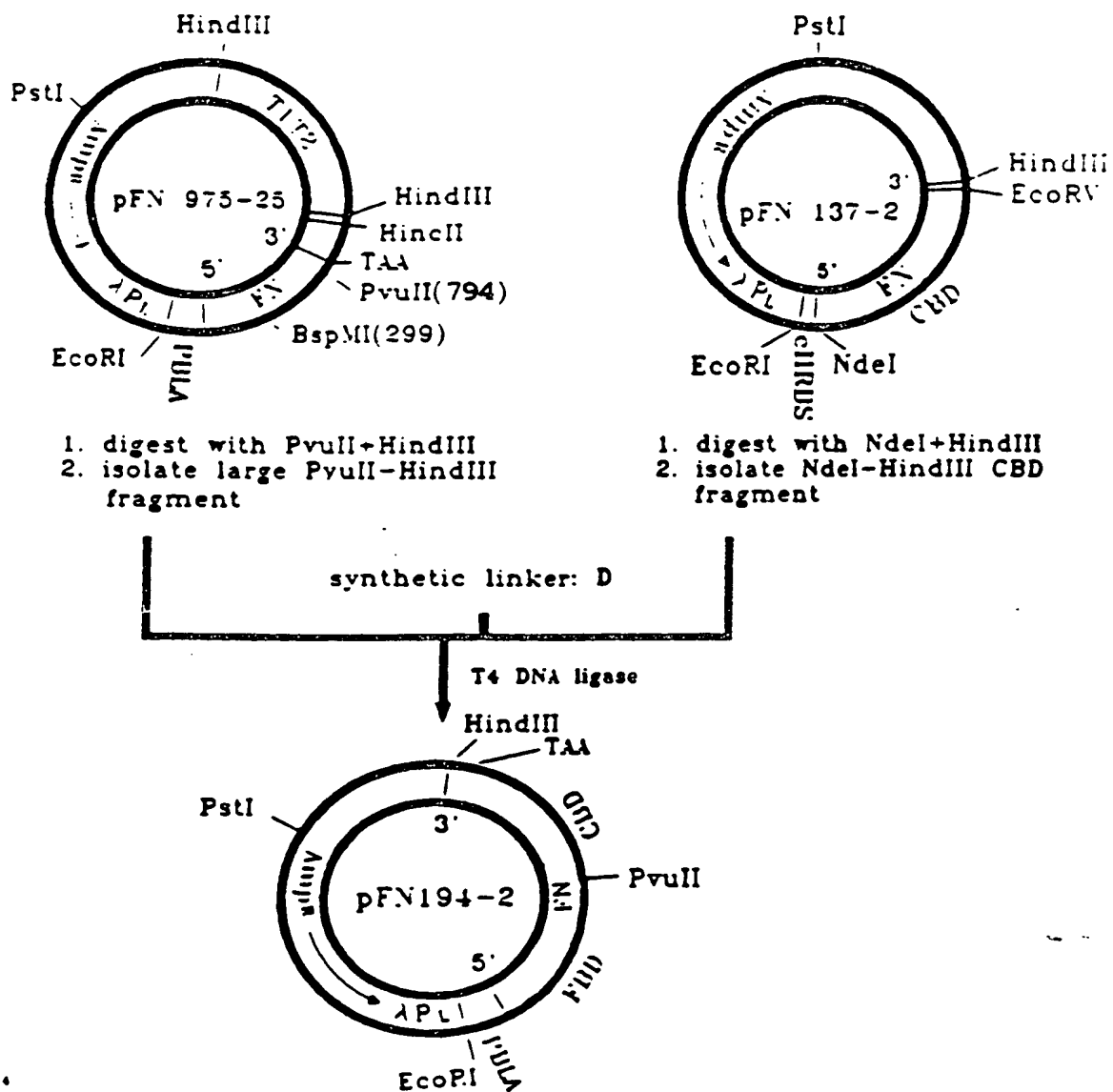


Figure 41

A 5' GGGCTGGGCGAGGGAGAATAAGCTGTACCATCGCAAACCGCTAACAGCTGA 3'  
3' ACCCGCTCCCTCTTATTTCGACATGGTAGCGTTTGGCGATTGTCGACTTCGA 5'

B 5' GGGCTGGGCGAGGGAGAATAAGCTGTACCATCGCAAACCGCCATATGTAAA 3'  
3' ACCCGCTCCCTCTTATTTCGACATGGTAGCGTTTGGCGGTATACATTTTCGA 5'

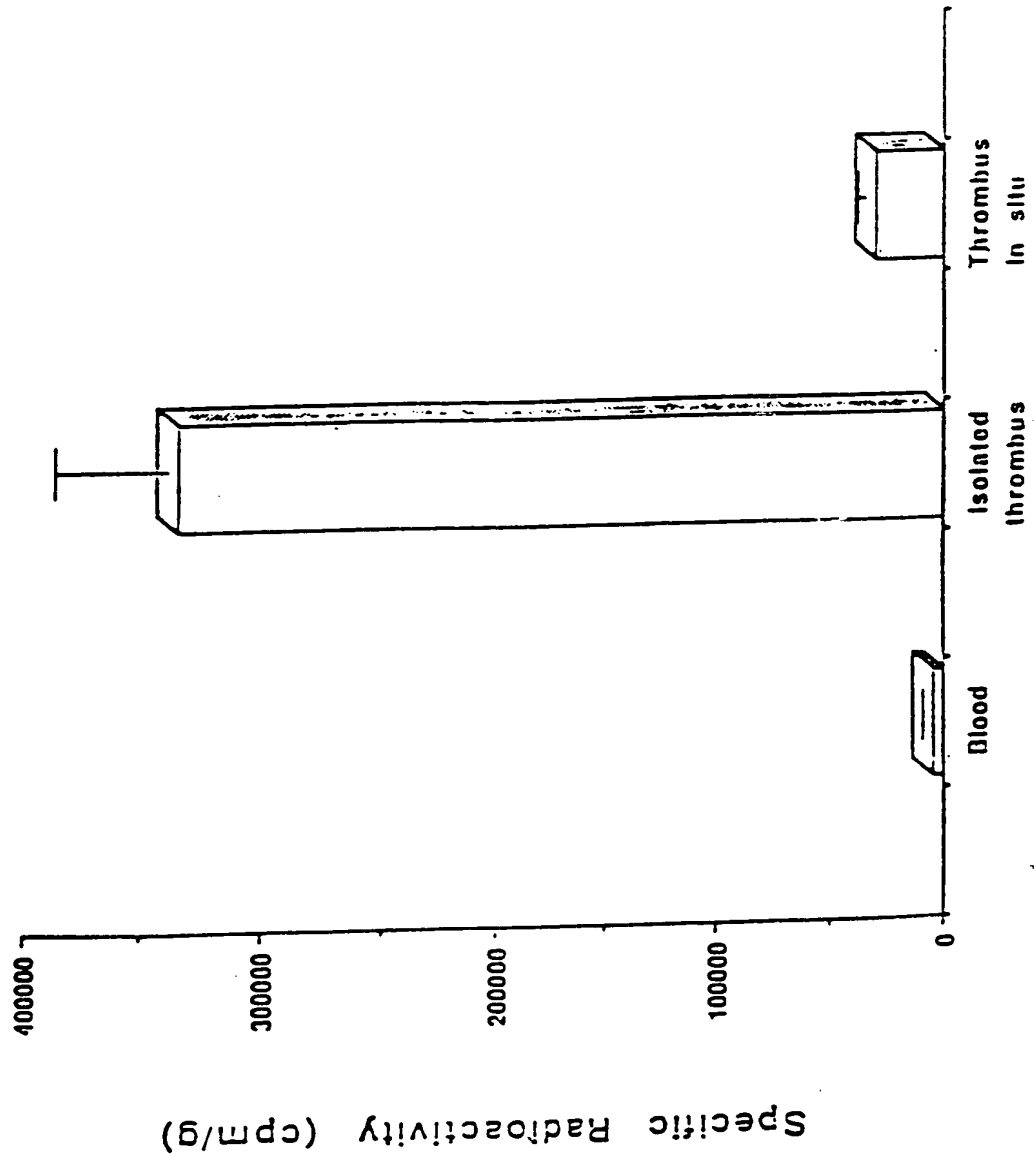
C 5' ATGGCCGTGGAGACAGCTAACAGCTGA 3'  
3' TACCGGCACCTCTGTCTGATTGTCGACTTCGA 5'

D 5' CTGTATACCAACC 3'  
3' GACATATGGTTGGAT 5'

002210" T 2626460

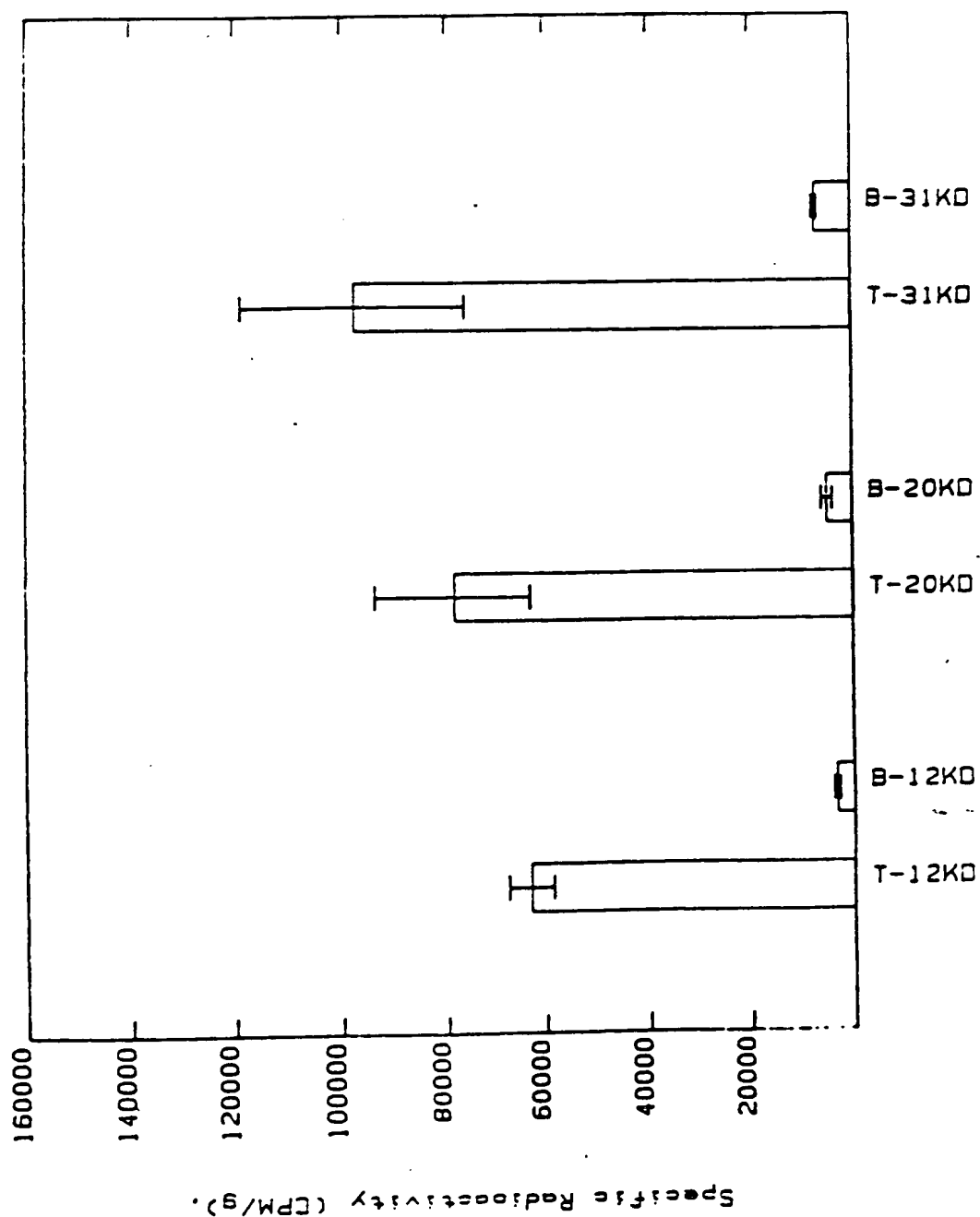
Figur 42

# Uptake of Labeled 31KD rFBD by Blood Clots in the Rat Coil Model



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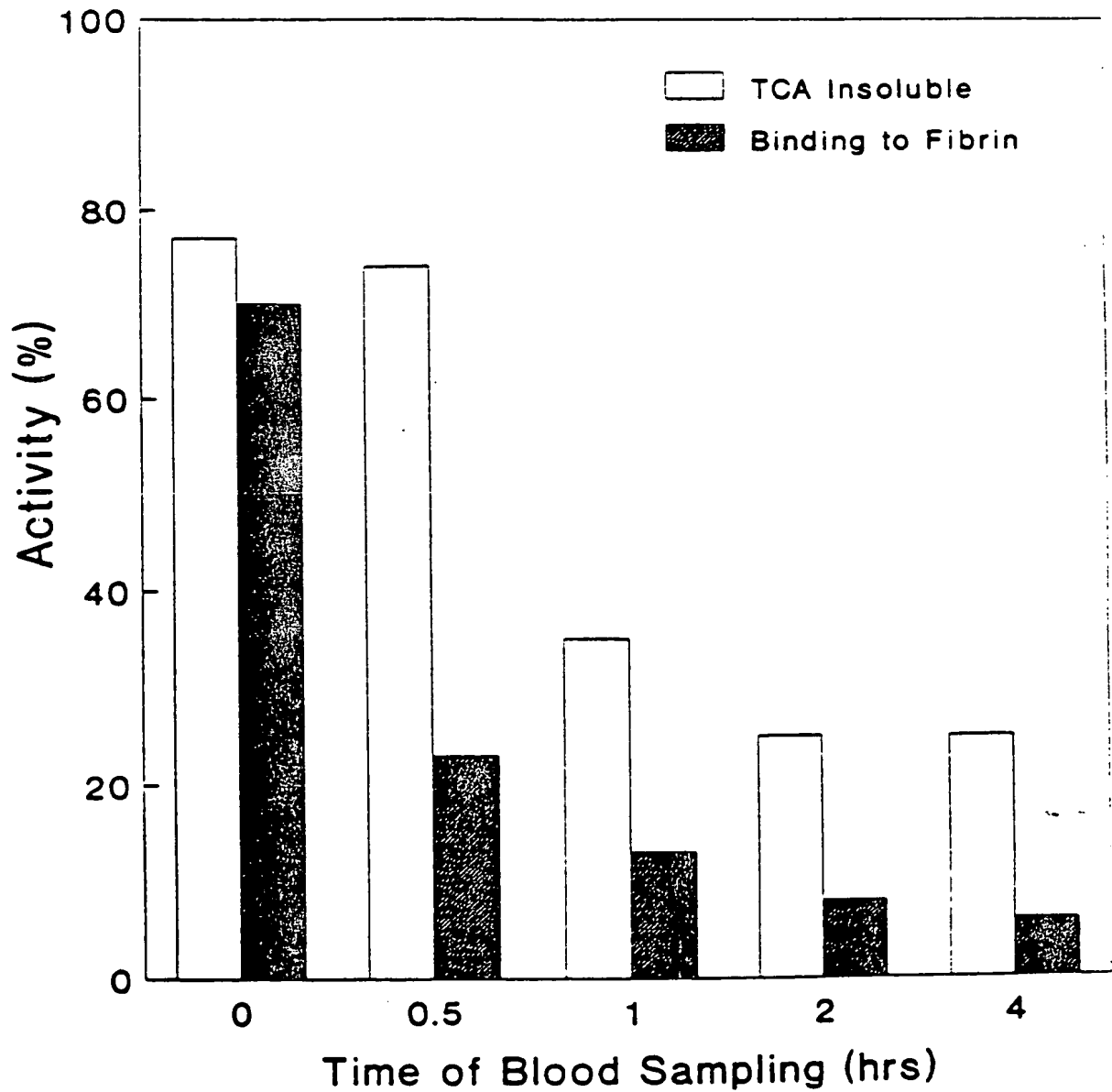
Figure 43  
COMPARISON BETWEEN 12, 20 & 31KD FBD MOLECULES



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Figure 44

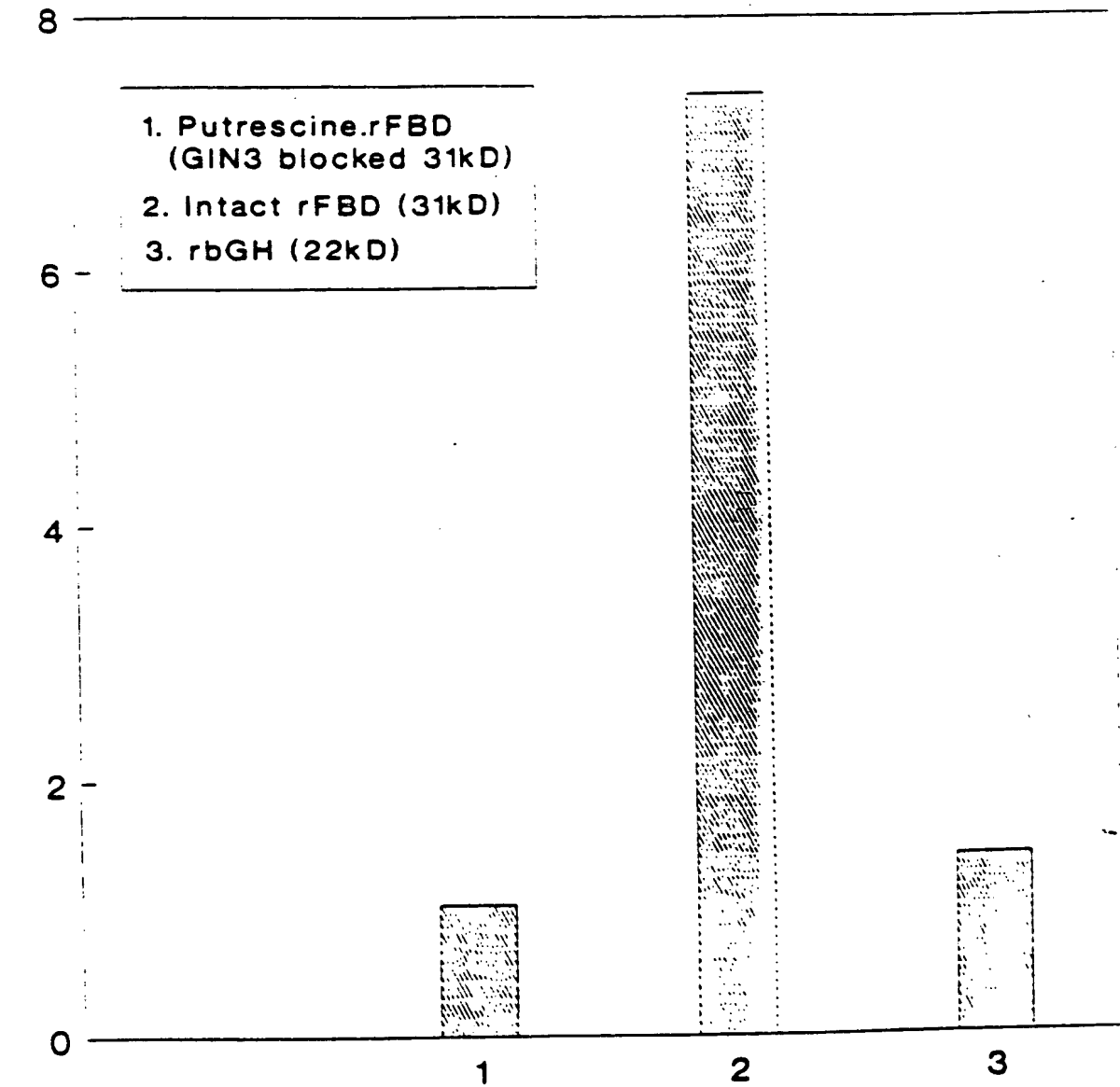
Metabolic Stability of rFBD in Rats;  
Ex-vivo Binding to Fibrin vs. TCA  
insolubility



ti-3/6/2

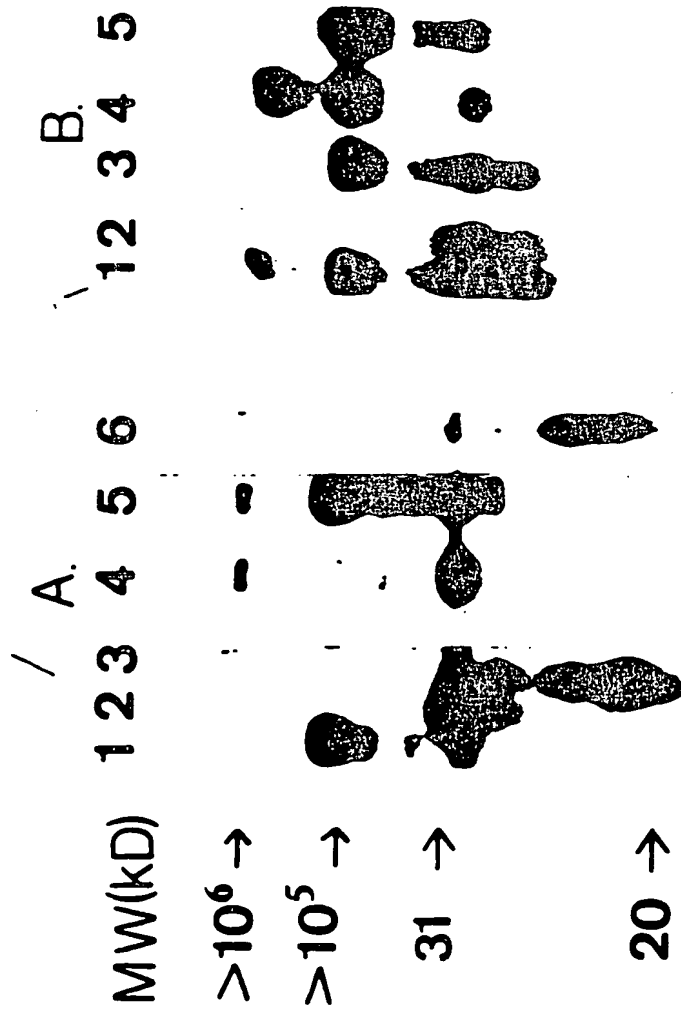
Figure 45

Specificity of binding to Fibrin;  
Effect of T.G. on the binding of  
rFBD vs. rbGH (Reaction II)



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Figur 46



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Figure 47

Binding of FBD to preformed clot ( Reaction II);  
Effect of FN and Heparin.

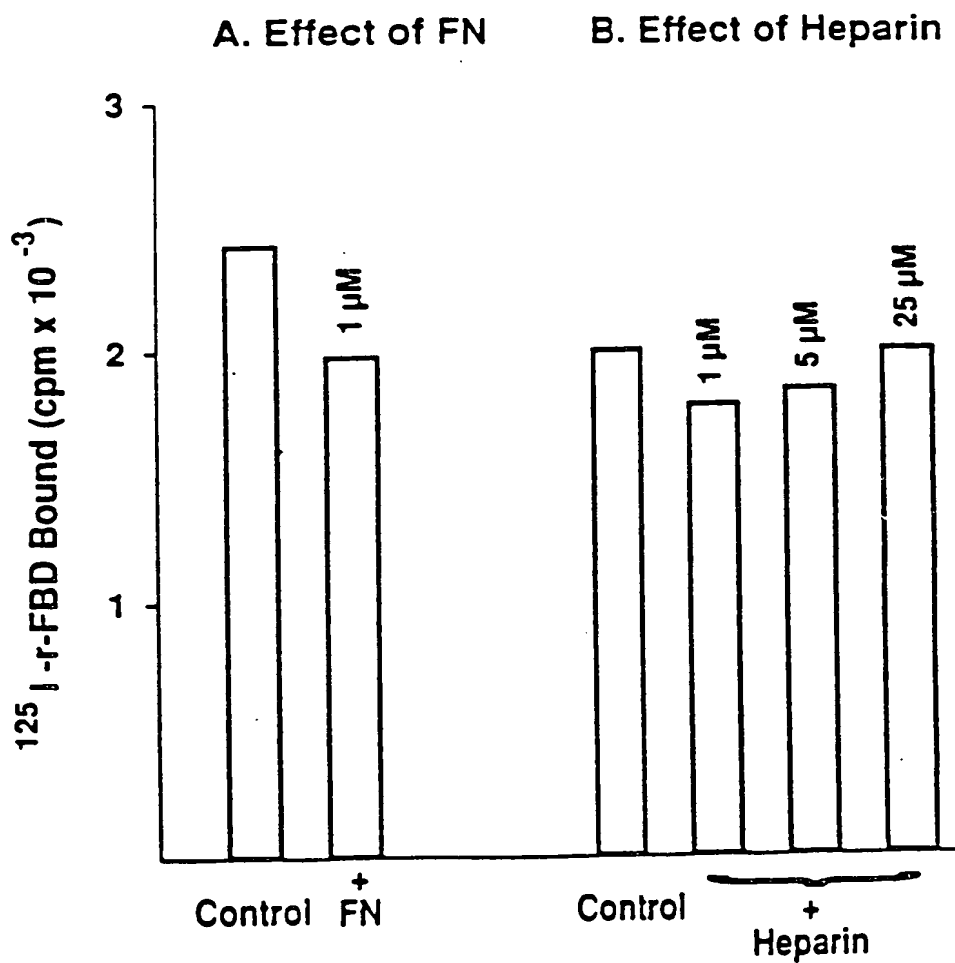
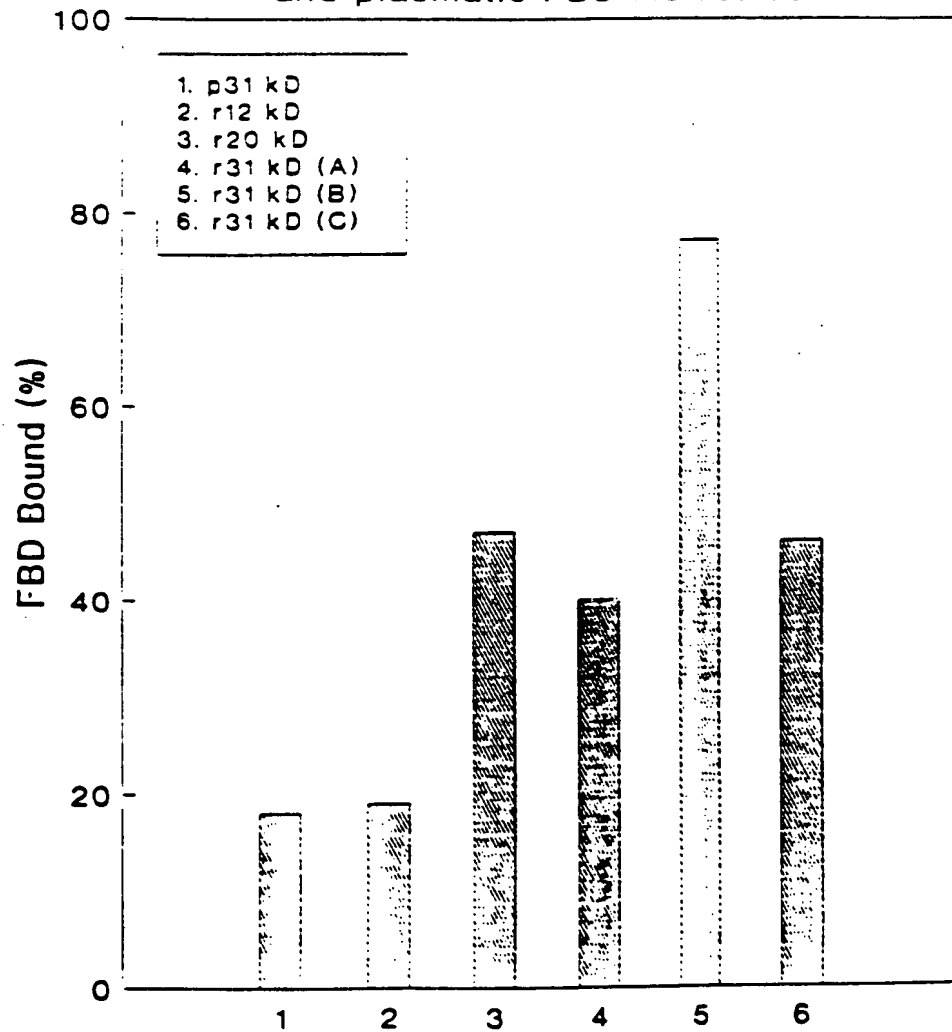


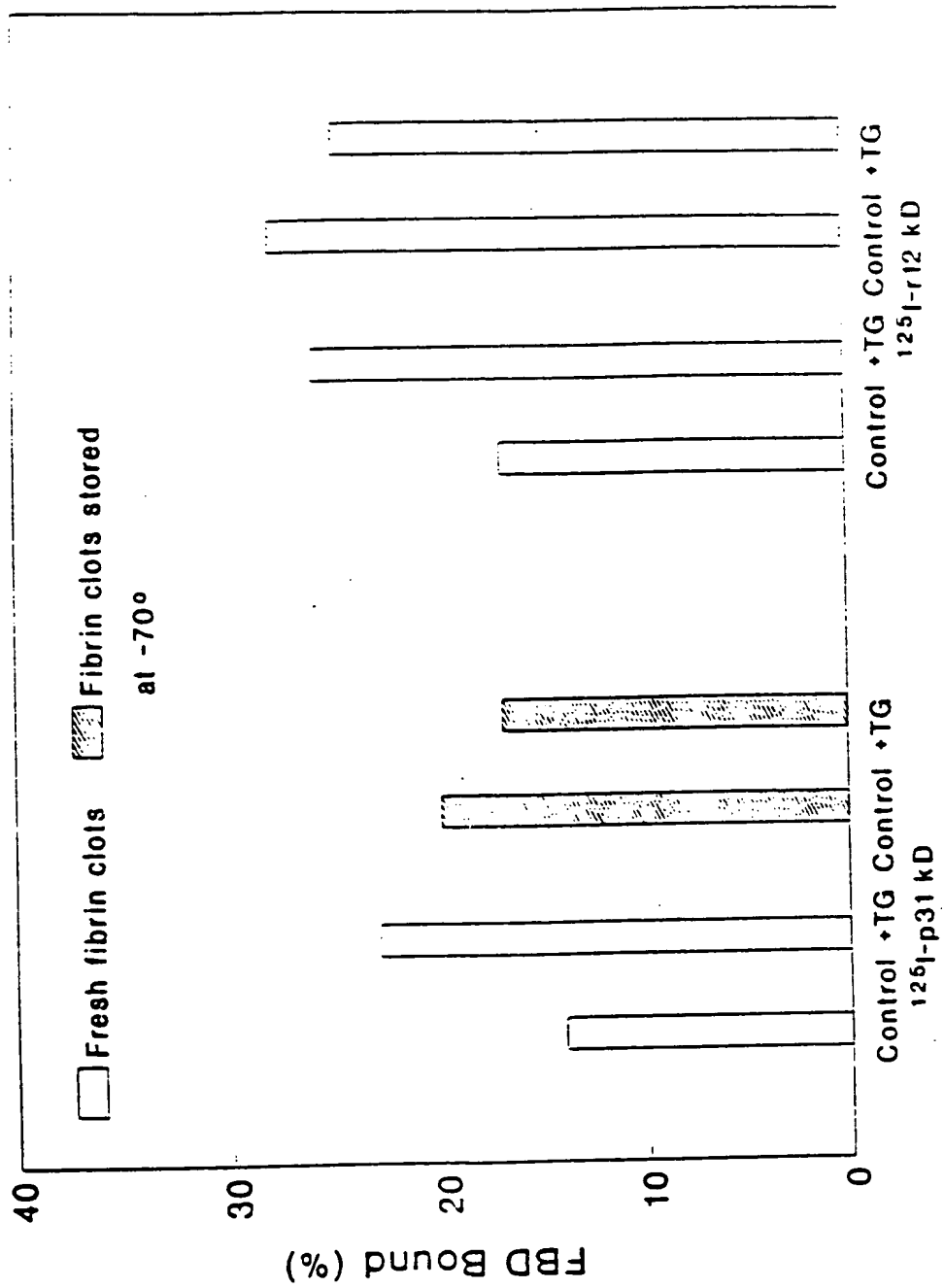


Figure 48

Binding of FBD to Fibrin clot (reaction II);  
comparison between various recombinant  
and plasmatic FBD molecules



Binding of FBD to Fibrin clot (reaction II);  
Comparison between fresh and frozen Fibrin clots

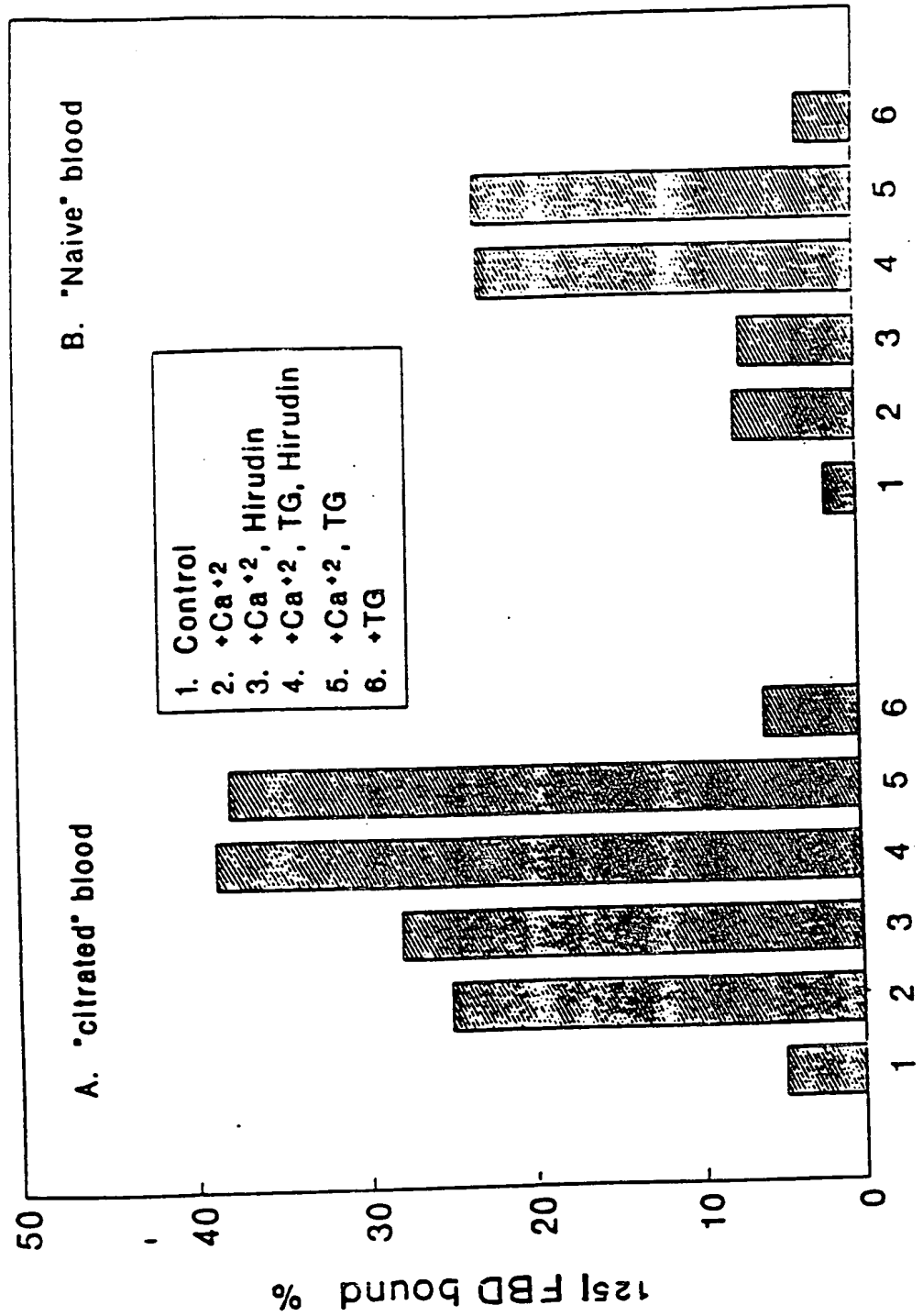


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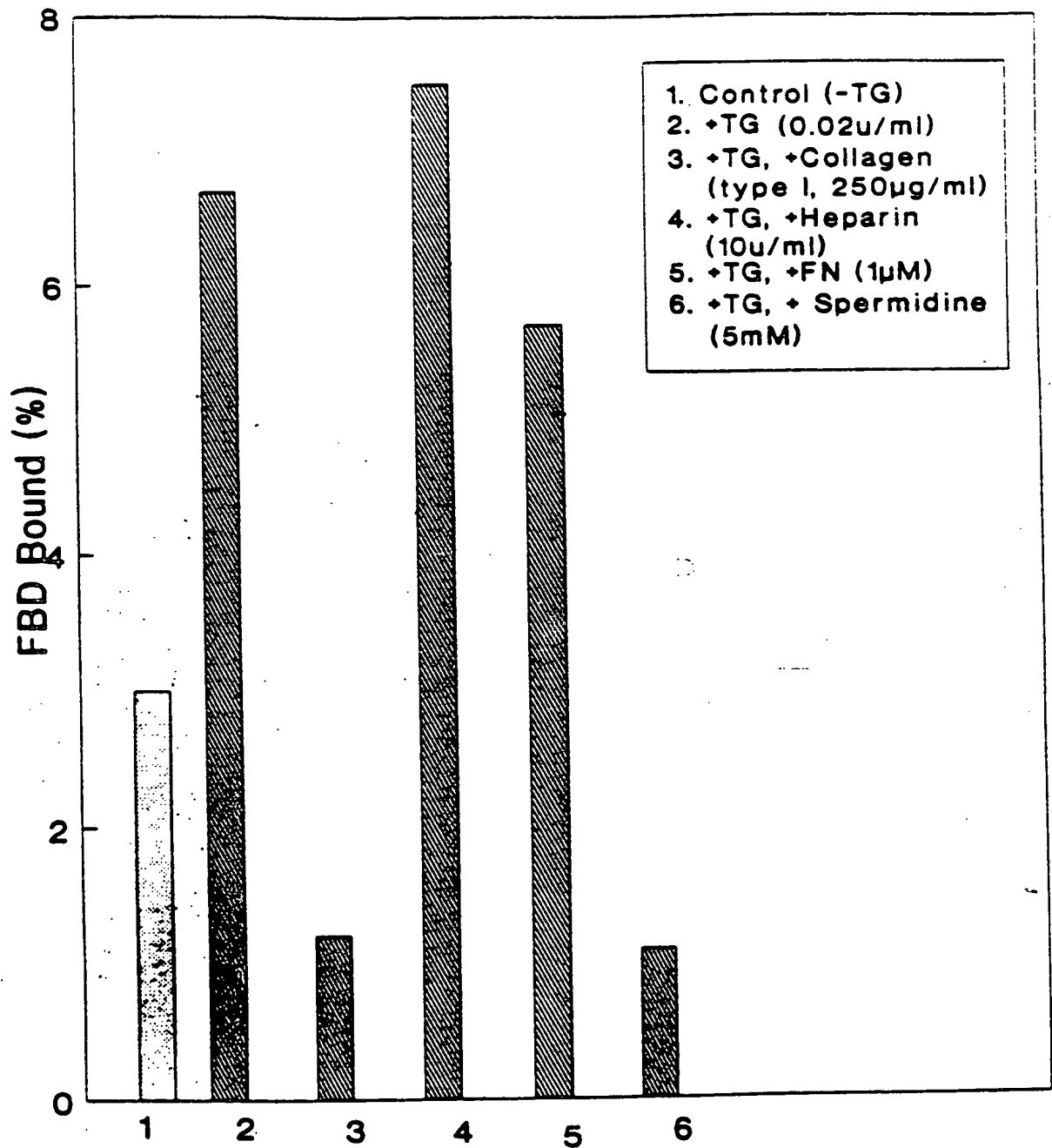
Figure 50

# Binding of FBD to Fibrin (Reaction II)



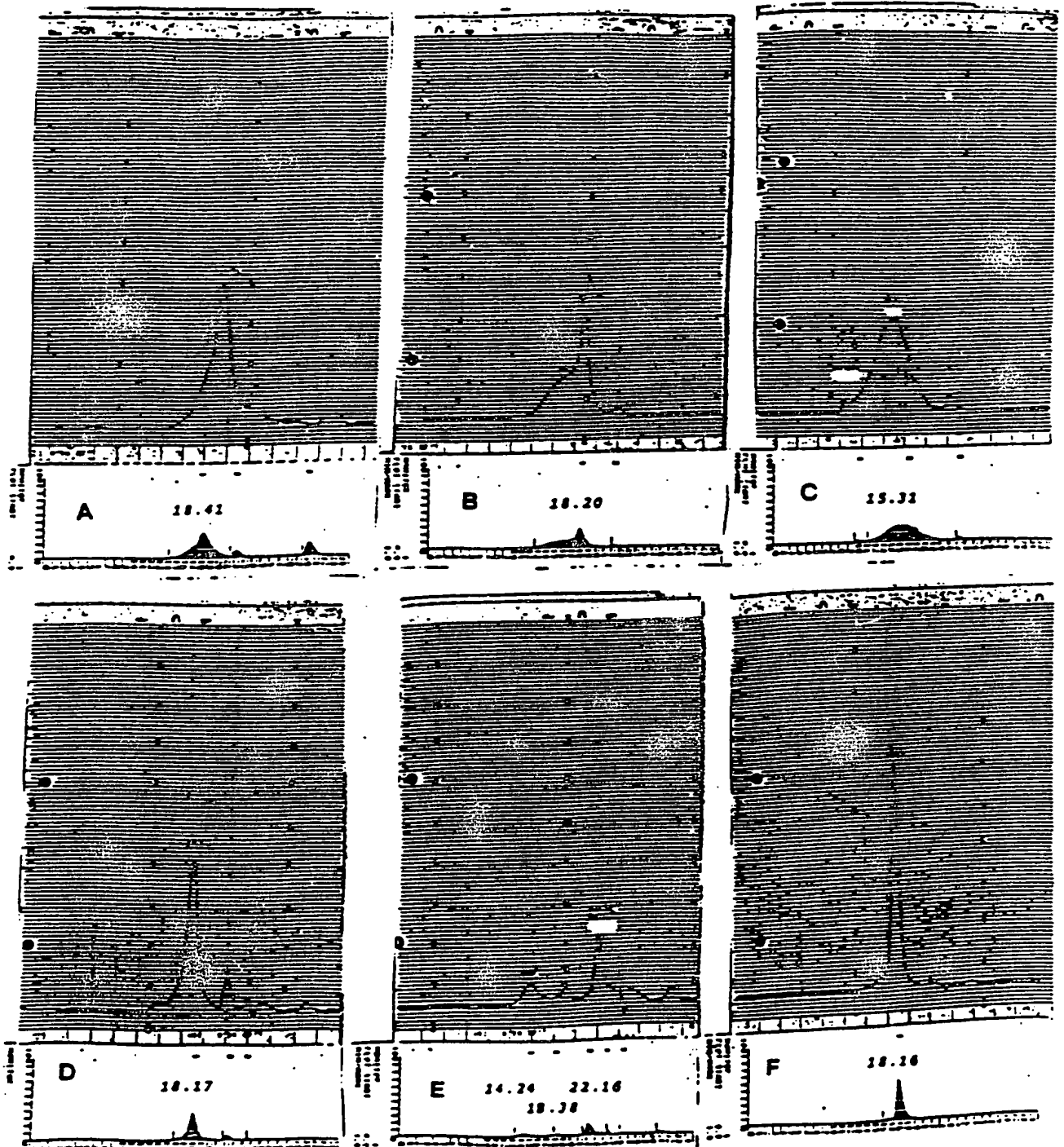
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## r-FBD binding to ECM



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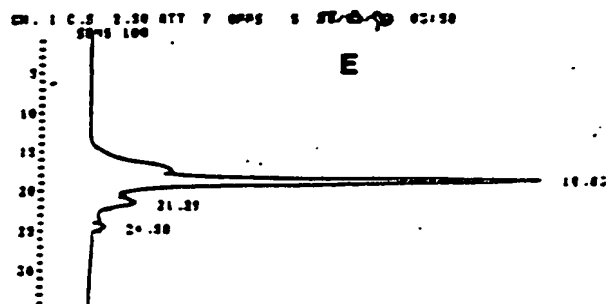
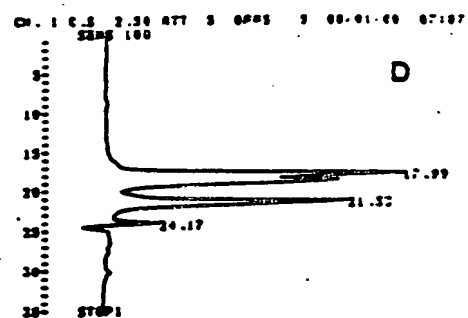
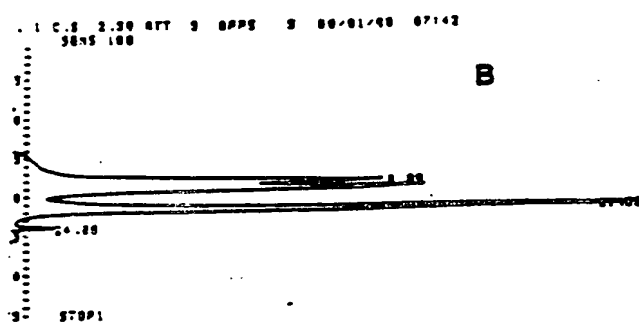
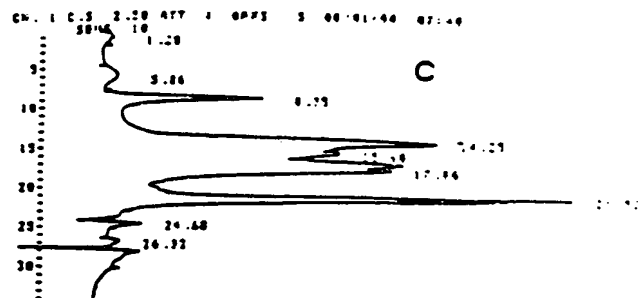
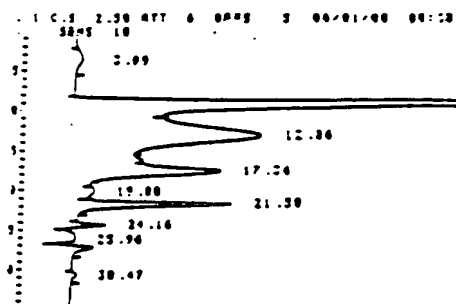
Figure 52



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Figure 53



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